PALLADIUM CATALYZED CROSS-COUPLING REACTIONS OF ALLYL- AND VINYLSILANES

BY

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THESIS

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Abstract

Palladium-catalyzed cross-coupling of γ-substituted allylic silanolates with aryl bromides was investigated. It was discovered that γ-selectivity is heavily influenced by the substituents at silicon. It is proposed that undergoing an activated pathway significantly lowers the selectivity of the reaction. A major side-product of this reaction was discovered and conditions were developed to suppress the undesired reaction. It is proposed that the side reaction shares at least two intermediates with the desired cross-coupling reaction. The use of arsenic ligands and elevated temperatures mildly suppressed the side-reaction and further studies are needed to completely prevent the unwanted pathway from occurring.

The development and application of a 1,2-differentiated bissilylethene moiety has been studied. Moderate yields are obtained in the fluoride-free coupling with aryl iodides under mild conditions. When the cross-coupling reaction is conducted with aryl bromides poor yields of the desired product are obtained. The reactive silanolate species was discovered to dimerize to a non-competent disiloxane species at elevated temperatures. Hemilabile phosphine ligands and basic additives can be employed to facilitate the cross-coupling with aryl bromides; however, further studies are needed to prevent dimerization of the silanolate from occurring.

“Keep on beginning and failing. Each time you fail, start all over again, and you will grow stronger until you have accomplished a purpose - not the one you began with perhaps, but one you'll be glad to remember.”

-Anne Sullivan

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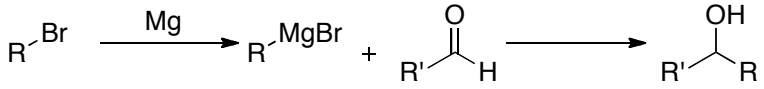
Chapter 1. Allylic Cross-Coupling Reactions

1.1. Introduction

The creation of carbon-carbon (C-C) bonds is fundamental to the study of organic chemistry. One of the earliest methods to synthesize C-C bonds is through the union of organomagnesium reagents and carbon electrophiles.[1] Grignard reactions have become a fundamental transformation in organic chemistry, allowing the ready creation of carbon-carbon bonds from organometallic reagents and carbon electrophiles (Scheme 1).

Scheme 1



Despite the generality of the Grignard reaction, its application to complex molecule synthesis is severely limited by the low chemoselectivity of organomagnesium compounds due to their high reactivity.[2] This problem was circumvented by the discovery of transition metal-catalyzed cross-coupling reactions wherein, a highly reactive organic nucleophile can be generated *in situ*. Initial discoveries demonstrated that using an appropriate transition metal catalyst, aryl-, alkynyl-, and alkenyl bromides can undergo cross-coupling reactions with organotin (Stille), organozinc (Negishi), organoboron (Suzuki) and organosilicon (Hiyama-Denmark) compounds.[3] Since this initial discovery, numerous conditions have been reported to limit the transition metal loading while still accomplishing the couplings under mild reaction conditions. Furthermore, studies have been designed to incorporate less toxic elements (tin) while still maintaining high reactivity and generality. Over the past 20 years great progress has

been achieved in the cross-coupling of aryl-, alkynyl, alkenyl, alkyl and allylic cross-coupling reactions.[3a]

1.2. Allylic Cross-Coupling Reactions

Allylation reactions constitute an important class of chemical transformations because the products of the reactions not only contain a newly formed carbon-carbon bond but also a reactive olefin moiety for further functionalization.[3b] Also, allylated arenes constitute an important structural motif in organic chemistry due to many natural products that posses this functionality.[3b,4]

Two heterolytic disconnects are possible for allylated arenes. One (Figure 1, path a) consists of allylic electrophile and one (Figure 1, path b) in which the allyl group is a nucleophile. The electrophilic allyl cation is typified by the Friedel-Crafts reaction. While straightforward and atom economical, the Friedel-Crafts reaction suffers from low site-selectivity and harsh reaction conditions. Also, the scope is limited to sufficiently nucleophilic arenes. The more synthetically useful transformation of this type utilizes metalloarenes as nucleophilic donors with allylic electrophiles in cross-coupling reactions. This type of disconnection has been thoroughly described for nucleophiles bearing boronic acids.[5] Despite this synthetic advance over Friedel-Crafts reactions it is often difficult to predict the site-selectivity due to the π–allylpalladium intermediate observed after oxidative addition to the allylic electrophile. However, the second principle disconnect (Figure 1, path b) can alleviate this problem by utilizing aryl electrophiles with nucleophilic allyl moieties. This type of cross-coupling reaction eliminates the issue of site-selectivity observed with the former approach because the π-allylpalladium intermediate can only be formed following the transmetalation step.

Because reductive elimination is facile the π-allyl intermediate is not readily formed and the selectivity-determining step is commonly the transmetalation event. This type of cross-coupling has been accomplished with a variety of different organo magnesium, tin, boron, and silicon nucleophiles.

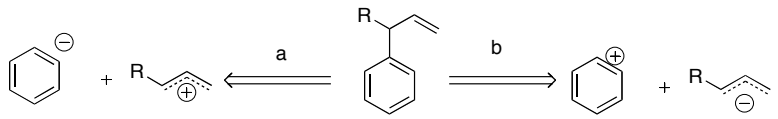


Figure 1. Retro-Synthetic Analysis of Allylated Arenes.

Despite the aforementioned problems of low chemoselectivity of organomagnesium reagents, any of the above organometallic compounds are suitable substrates for undergoing simple allylic cross-coupling reactions with aryl bromides. The largest discrepancy between reagents arises when the allylic nucleophile contains substitution at the γ-position. Due to the substitution of the nucleophile, a mixture of isomeric products can be obtained from the cross-coupling reaction (Figure 2). These substituted allylic nucleophiles have been extensively studied with the various metal donors.

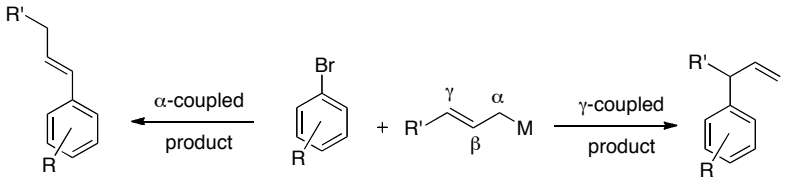
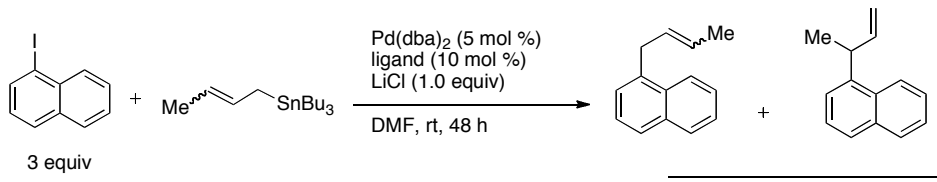


Figure 2. Substituted Allylic Nucleophiles.

Allyl- and crotylstannanes are among the first substrates to undergo this transformation with a variety of aryl triflate electrophiles. The seminal work afforded the

desired cross-coupled products in low yields and selectivity.[6] Further studies performed by Tsuji and coworkers discovered that the selectivity of the cross-coupling was highly dependent on the ligand used in the reaction (Scheme 2). It was observed that the use of triphenylarsine (Ph_3As) furnished products with high α-selectivity; however, when triphenylphosphine (Ph_3P) or tri(2-furyl)phosphine was used, high γ-selectivity was observed.[7] Choice of ligand has proven to be a critical factor in obtaining high selectivity in these cross-coupling reactions as well as Suzuki and Hiyama-type allylic cross-couplings.

Scheme 2

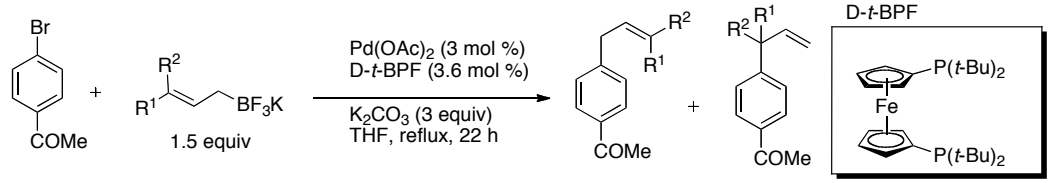


ligand	yield, %	ratio (α:γ)
Ph_3As	61	91:9
Ph_3P	23	0:100
$(2\text{-furyl})_3P$	71	15:85

Allylboronic acids and esters have been employed to obtain modest selectivity of both α– and γ-coupled products.[8] Although the substrate scope for the allylic boronic acids was fairly limited, the use of substituted allylic trifluoroborate derivatives has been shown to increase selectivity as well as scope with respect to the nucleophile (Scheme 3).[9] Excellent yields and selectivities were obtained with a variety of γ-substituted allylic borates. As observed with allylic stannanes, yields and selectivities are highly dependent on choice of ligand. In these cases monodentate Ph_3P and bidentate phosphines possessing small bite angles affords products in low yields and selectivity. Alternatively, bidentate phosphines with large bite angles (e.g. 1,10-bis(di-t-butylphosphino)ferrocene

(D-*t*-BPF)) afford products with high yields and selectivity. Despite the broad scope of competent organoborate derivatives, relatively few aryl bromides were highlighted in the cross-coupling reactions of γ-disubstituted allylic trifluoroborate salts.[9c]

Scheme 3

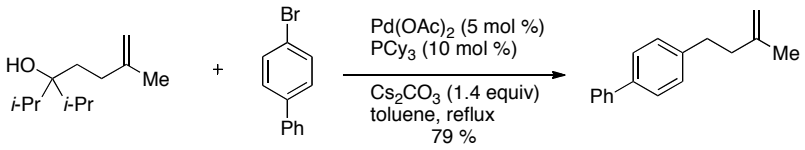


R^1	R^2	yield, %	ratio (α:γ)
Me	H	99	1:99
Ph	H	99	1:99
n-Bu	Me	99	1:99

Recently homoallylic alcohols have been employed as a nucleophilic allyl donor in cross-coupling reactions with aryl bromides (Scheme 4).[10] The mechanistic proposal for this transformation is described as displacement of the aryl-palladium-bromide complex by the homoallylic alkoxide anion. Retro-allylation of the alkoxide palladium intermediate to produce a ketone by-product as well as a diorganopalladium intermediate, which, after facile reductive elimination, affords the desired product. The substitution pattern on the starting homoallylic alcohol not only influences the reactivity of the substrate but also dictates the olefin geometry of the products leading authors to conclude that the retro-allylation is occurring through a six-membered "chair-like" transition state. γ-Substituted homoallylic alcohols significantly lower the reaction rate and significantly lower yields of the products are obtained when a methyl group is present at the γ-position. Despite the advance of using a nucleophilic substrate devoid of metal

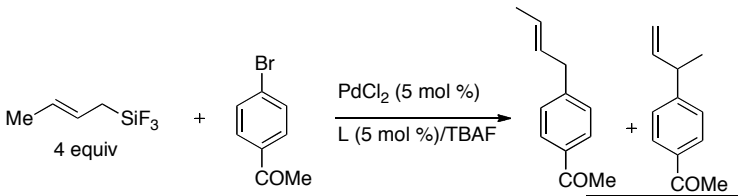
reagents, the stoichiometric ketone by-product as well as the limited nucleophilic scope make this a less attractive method for installing an allyl moiety.

Scheme 4



One of the most selective coupling methods employs allylic trifluorosilanes as coupling partners. Hiyama observed that allyl-, crotyl- and γ-substituted allylic trifluorosilanes undergo cross-coupling with a variety of aryl bromides to afford the desired product in high yields and selectivity.[11] The selectivity of the reaction is highly dependent on the ligand used. Employing Ph_3P as a ligand provides high γ-selectivity; however, using bidentate phosphine ligands with small bite-angles (1,3-bis(diphenylphosphino)propane (dppp)) provided high yields of α-substituted products (Scheme 5). As with the previous methods, this example demonstrates a powerful ligand effect on the selectivity of these cross-coupling reactions; an effect that will manifest itself throughout the optimization of allylic-silanolate cross-coupling reactions.

Scheme 5



L	yield, %	ratio (α:γ)
Ph_3P	97	0:100
dppp	92	99:1

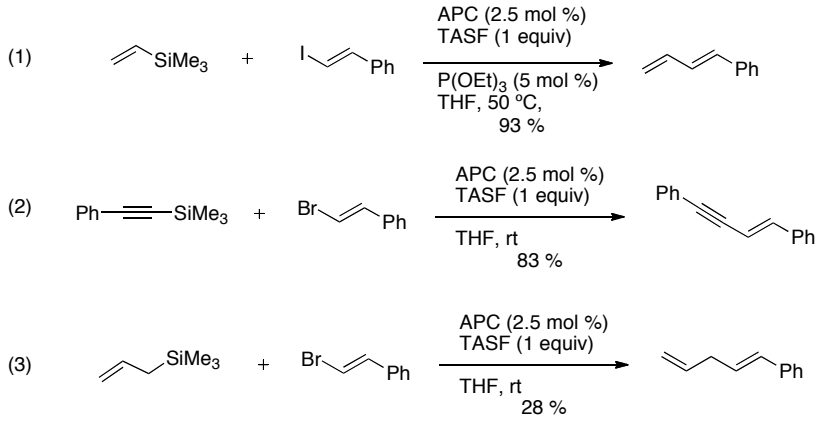
Chapter 2. Silicon-Based Cross-Coupling

2.1. Introduction to Silicon Based Cross-Coupling

The discovery of palladium-catalyzed cross-coupling reactions has significantly impacted not only the academic community but also the chemical industry. The ease with which carbon-carbon bonds can be synthesized employing transition metal cross-coupling reactions has led to its widespread use in medicinal chemistry.[3b] Classically, tin and boron containing compounds have accomplished these cross-coupling reactions in high yields under mild conditions.[3] However, these compounds are not without several shortcomings. The use of stoichiometric toxic reagents is a severe limitation to organotin chemistry,[12] and often organoboron reagents suffer from a lack of stability and protiodeborylation occurs.[13] In few of these limitations the Denmark group has been exploring the utility of organosilicon compounds as nucleophiles in cross-coupling reactions.[14] Hiyama and co-workers seminal publications demonstrated that organosilanes are effective nucleophiles in cross-coupling reactions. By employing silicon reagents, the use of stoichiometric toxic tin compounds can be avoided.[15] Alkenyl-, alkynyl-, and allyltrimethylsilanes were the first reagents described to be competent coupling partners with fluoride as an activator (Scheme 6).[15] Tris(diethy1amino)sulfonium difluorotrimethylsilicate (TASF) can be used as the fluoride source to form a pentacoordinate silicate thus increasing the polarization of the carbon-silicon bond leading to a more facile transmetalation. Greater application has since been discovered by incorporating heteroatoms at silicon to increase the carbon-silicon bond polarity. The use of the trialkoxy- or difluorosilanes has greatly improved

the scope of the cross-coupling reactions leading to more challenging biaryl cross-coupling reactions.[11,16] The permutations about the silicon center continue to be explored in efforts to address the shortcomings associated with silicon-based cross-coupling (e.g. fluoride promoted reactions limit functional group compatibility).

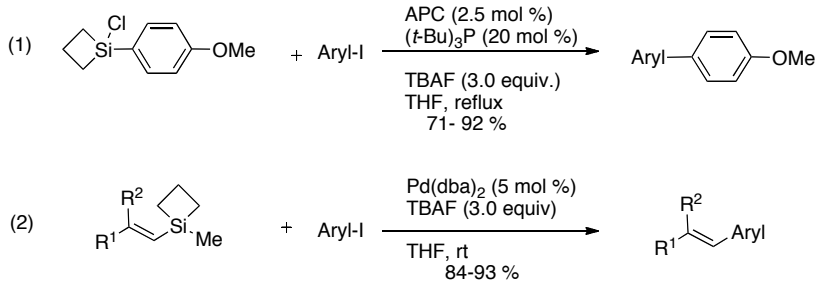
Scheme 6



Seminal work from the Denmark laboratories focused on the use of silacyclobutanes as substrates in cross-coupling reactions due to their ease of synthesis and increased Lewis-acidity.[17] While the use of these reagents did not alleviate the need for a fluoride source to promote the coupling, it did provide a starting material that was easily synthesized, purified and isolated. Aryl- and alkenylsilacyclobutanes were the first reagents prepared and used for cross-coupling reactions (Scheme 7).[17-18] Silacyclobutanes are thought to be highly Lewis acidic due to the strain-release involved in the rehybridization at silicon.[17] This increased Lewis acidity allowed for a more polarized carbon-silicon bond that results in a more facile transmetalation during cross-coupling reactions. It was originally proposed that fluoride ion would bind to the silicon forming an unstable pentacoordinate silicate species. The strain release arises from the shift in

tetrahedral to trigonal bipyramidal geometry about the silane. This pentacoordinate silicate was proposed to be the intermediate that induced the transmetalation event.

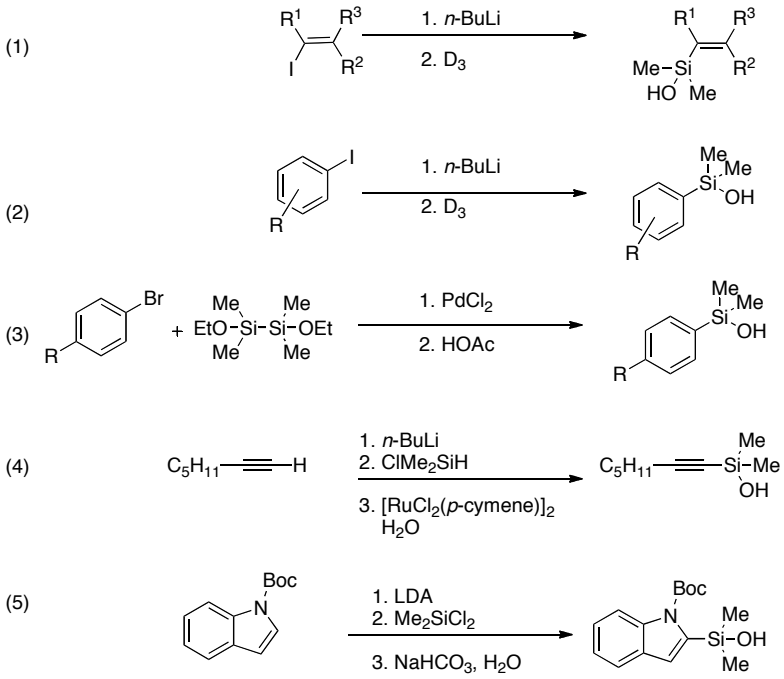
Scheme 7



Subsequent studies revealed that the silacyclobutanes suffered from rapid ring opening in the presence of fluoride to afford mixtures of silanol and disiloxane species.[19] This silanol species was isolated and subjected to the coupling conditions independently from the parent silacyclobutanes. Surprisingly, this compound is also competent in the palladium-catalyzed cross-coupling with aryl halides under fluoride activation and studies to synthesize, isolate, and apply organosilanols to these reactions were undertaken.

The usefulness of the organosilanols derives from their ability to be incorporated into a variety of organic structures (Scheme 8).[20] Alkenyldimethylsilanols undergo the fluoride promoted cross-coupling with a variety of aryl- and alkenyl electrophiles.[20a,20d,21] Additionally, (α-alkoxyvinyl)silanols cross-couple with aryl iodides under similar conditions.[22] To further illustrate the utility of organosilanols in cross-coupling reactions, fluoride-free coupling conditions were developed to increase the substrate compatibility in cross-coupling reactions.

Scheme 8

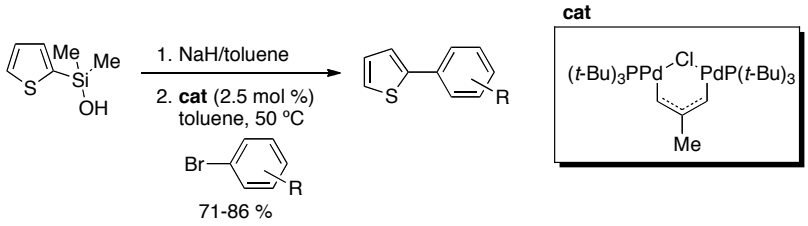


2.2. Utility of Organosilanols Under Fluoride-Free Coupling Conditions

Organosilanols and silanolates are attractive reagents due to their ease of synthesis, low toxicity, but most importantly because they can be activated under fluoride-free coupling conditions. Alkenyl-,[23] aryl-,[24] alkynyl-,[20b] and heteroarylsilanols[25] undergo palladium-catalyzed fluoride-free cross-coupling reactions with a plethora of aryl halides. To conduct fluoride-free cross-coupling reactions with organosilanols a Brønsted base is required, presumably to deprotonate the silanol and form the nucleophilic silanolate salt. Preliminary mechanistic investigations revealed that following oxidative addition to afford the aryl-palladium-X species, displacement of the halide ligand occurs forming an Si-O-Pd linkage.[26] It is this species that undergoes the rate-determining transmetalation event prior to facile reductive elimination to afford the desired cross-coupled product. On the basis of this early mechanistic insight it was

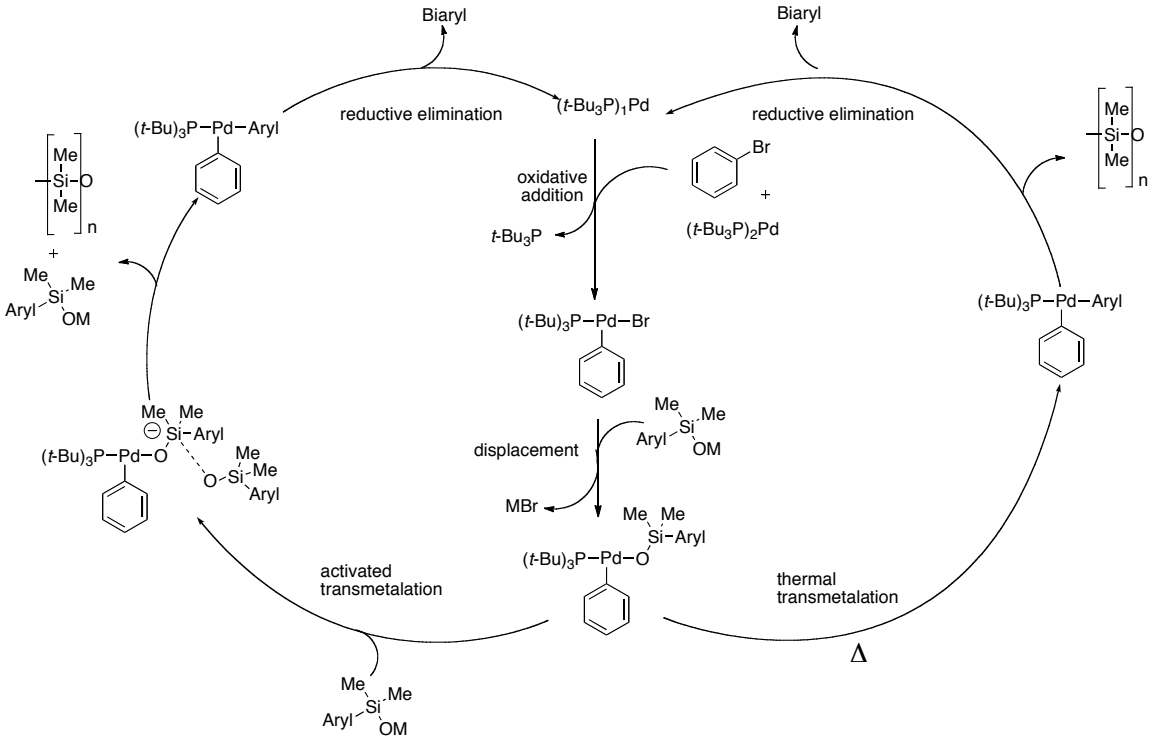
hypothesized that use of preformed silanolate salts would allow cross-coupling without the need for additional base. The use of a strong bases (KH, NaH, etc) led to the synthesis and application of heterocyclic silanolate salts toward cross-coupling with aryl iodides and bromides (Scheme 9).[27] Following this report aryl-,[28] alkenyl-,[29] and allylic[30] silanolates have been synthesized and isolated for the use in cross-coupling reactions.

Scheme 9



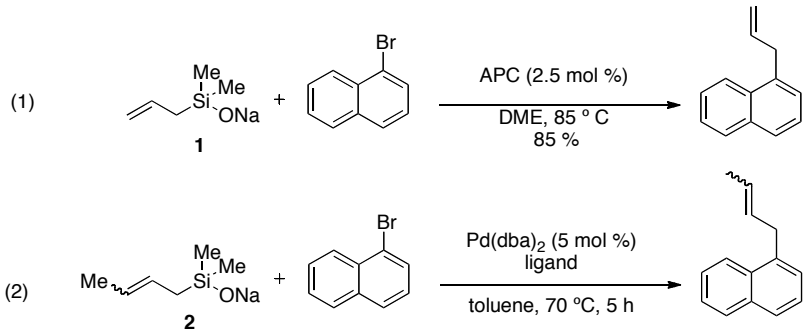
Mechanistic work from these laboratories has led to the proposal of silanolate cross-coupling reactions detailed in Scheme 10.[31] As stated above, following oxidative addition of the palladium(0) species to the aryl halide, nucleophilic displacement of the silanolate occurs at palladium. Derivatives of this aryl-palladium-siloxy species have been isolated and studied in order to elucidate the mechanism of transmetalation.[31] Transmetalation can follow two pathways: (1) thermal activation (8-Si-4) occurs *via* heat transfer to induce a transmetalation event and/or (2) anionic activation (10-Si-5) at the silicon center (added base or excess silanolate salt) proceeds through a discreet silicate intermediate destabilizing the intermediate and raising the nucleophilicity of the *ipso*-carbon. The destabilization and enhanced nucleophilicity increases the rate of transmetalation to palladium. Following transmetalation facile reductive elimination occurs to afford the desired cross-coupled product and simultaneously forming palladium(0) to complete the catalytic cycle.

Scheme 10



On the basis of the previous success that employed organosilanols as coupling partners we envisioned the use of allyl groups as the transferable group in cross-coupling reactions. Sodium allyldimethylsilanolate, **1**, and sodium 2-butenyldimethylsilanolate, **2**, were prepared and used in the palladium catalyzed cross-coupling of aryl bromides (Scheme 11).[30] With bis(dibenzylideneacetone)palladium ($Pd(dba)_2$) and norbornadiene (nbd), as a ligand, good γ-selectivities and yields were obtained for the cross-coupled products. As previously reported by Hiyama, a significant ligand effect is observed in this coupling reaction. Olefinic ligands provided the highest γ-selectivity while phosphine ligands provide only slight preference for the branched products (γ) compared to the linear products (α).

Scheme 11



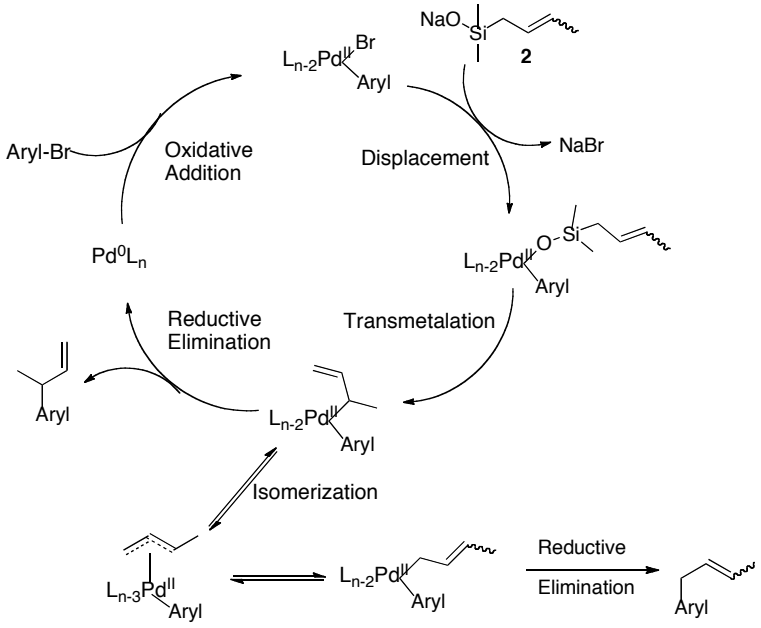
L	conversion,[a] %	ratio (α:γ)
Ph_3P	59	1:5
Cy_3P	47	1:6.3
nbd	53[b]	14:1

a) Based on GC results using biphenyl as internal standard

b) Isolated yield

The allylic silanolate is proposed to undergo an S_E2' transmetalation and the selectivity determining step arises from a competition of π-allyl isomerization of the palladium complex (affording α-product) versus a direct reductive elimination to form the γ-product. It was thought that the π-acidic olefin ligand facilitates reductive elimination and prevents the π-allyl isomerization from occurring.

Scheme 12



Despite the broad scope with respect to the bromide the nucleophilic scope was left largely unexplored. The goal of this project was to synthesize and isolate γ-substituted allylic silanolates and apply them in cross-coupling reactions with aryl bromides. We chose to begin with isopropyl- and prenyl substrates in order to: (1) demonstrate branched aliphatic groups are competent coupling partners, (2) prepare products that contain a chiral centers and (3) prepare products containing a quaternary carbon in hopes to develop a catalytic asymmetric process.

Chapter 3. γ-Substituted Allylic Silanolates Cross-Coupling Reactions

3.1. Introduction

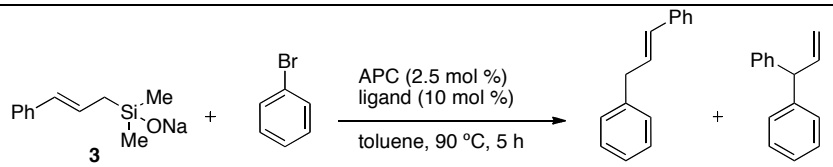
Recent reports from these laboratories have highlighted the utility of allylic silanolate salts and their ability to selectively undergo cross-coupling reactions with a myriad of aryl bromides.[30] Both unsubstituted sodium dimethylallylsilanolate (**1**) and sodium dimethylcrotylsilanolate (**2**) undergo facile cross-coupling with aryl bromides to give predominantly γ-coupled products in good yields and selectivities. The mechanism for this transformation was studied in detail as well as the stereochemical course for transmetalation using a chiral non-racemic allylic silanolate to better understand the stereodetermining step in order to develop a catalytic enantioselective process.[32] Despite these investigations, little was known about the scope of substitution tolerated in the coupling reaction of γ-substituted allylic silanolates. Variable substitution at the γ-position would increase the number of products available from the coupling. Additionally, γ-substitution places the new bond on the reactive carbon-center, it was hypothesized that these modifications could have great influence on the outcome of the coupling reaction.

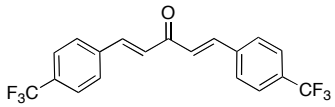
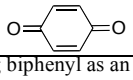
3.2. Background

Several γ-substituted allylic silanolates including alkyl and aryl substituents were originally prepared and tested in cross-coupling reactions. Sodium cinnamyldimethyl silanolate, **3**, was one of the first substrates tested and despite extensive screening of

palladium sources, ligands, and solvent, no conditions could be found that favored the desired γ-coupled product.[33] Only the linear or α-coupled product was obtained as the major isomer from these coupling reactions (Table 1).

Table 1. Cross-Coupling of Silanolate 3.

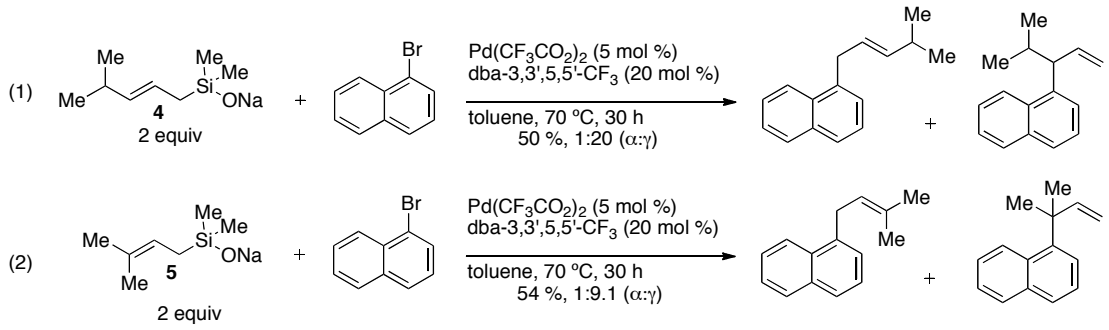


entry	ligand	yield,[a] (%)	ratio,[b] α:γ
1	Ph_3P	31	4.5:1
2	S-Phos	21	3.3:1
3		21	1.3:1
4		68	6.3:1

a) Determined by GC using biphenyl as an internal standard. b) Ratio determined by GC peak area of isomers

Sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate, (**4**), and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate, (**5**) were also used in the preliminary studies. These substrates contain aliphatic substituents at the γ-position and preliminary experiments employing different ligands, palladium precursors, and solvents gave positive results. Unlike the cinnamylsilanolate these substrates were able to provide the desired branched product in good selectivities and moderate yields. Palladium(II) trifluoroacetate, (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one, (dba-3,3',5,5'-CF_3) in toluene at 70 ºC were discovered to afford the highest γ-selectivity and yield of the desired products (Scheme 13).

Scheme 13



These preliminary reaction conditions provided good α:γ selectivities; however, the yields of the isolated products were moderate at best. The goal of this research project was to optimize the initial results to improve the yields and selectivities. Through many probing experiments it was concluded that many side reactions are competing during the course of this reaction and significant optimization will be required in order to prevent these unwanted side reactions from occurring (*vide infra*).

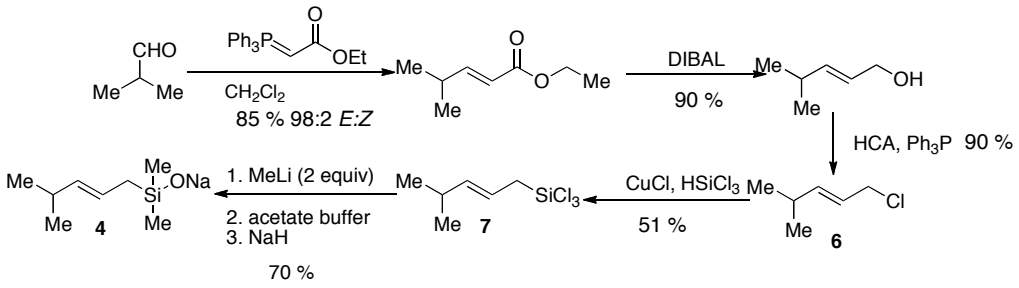
3.3. Results

3.3.1. Initial Results Employing Sodium (*E*)-Dimethyl(4-methylpent-2-en-1-yl)silanolate

The experiments conducted previously provided a good starting point for the optimization of cross-coupling reactions of γ-substituted allylic silanolates. Silanolate **4** was prepared in seven steps starting from isobutyraldehyde (Scheme 14). Wittig-olefination of isobutyraldehyde afforded the desired α,β-unsaturated ester in good yields (85 %) and *E*/*Z* (98:2) ratio.[34] Selective reduction of the ester resulted in good yield of the desired allylc-alcohol.[35] Because of the potential for isomerization to occur during chlorination hexachloroacetone (HCA) and triphenylphosphine were used for this step.[36]

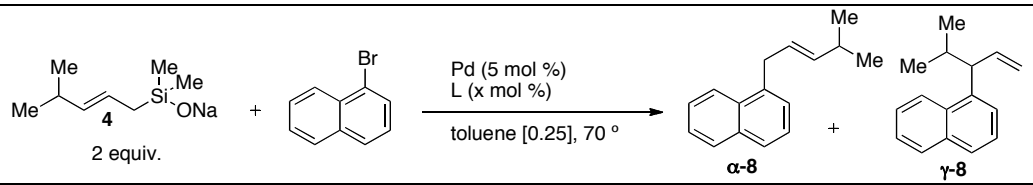
Copper-catalyzed silylation of the allylic chloride, **6** afforded the highly reactive allylic trichlorosilane, **7**, in moderate yields. Methylation (MeLi, 2.0 equiv) followed by hydrolysis with acetate buffer and deprotonation furnished the desired silanolate salt in good yields (70 %) over all steps.

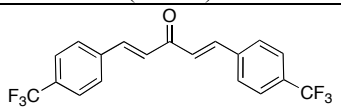
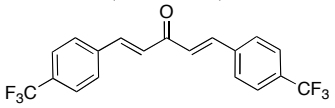
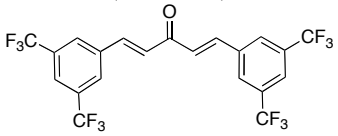
Scheme 14



To optimize the cross-coupling reaction and obtain high γ-selectivity, different palladium precursors with electron deficient olefin ligands were tested in the cross-coupling with 1-bromonaphthalene (Table 2). Using the electron deficient palladium source (palladium(II) trifluoroacetate) and (1*E*,4*E*)-1,5-bis(4-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (dba-4-4'-CF_3) high yields and γ-selectivities were observed. The yield of the reaction was moderately improved by using allylpalladium chloride dimer (APC) or $Pd(dba)_2$ as the palladium precursor. It was discovered that the γ-selectivity of this reaction was independent of olefin ligand as greater than 20:1 γ:α selectivity was obtained when using either dba-3,3',5,5'-CF_3, dba-4,4'-CF_3, or norbornadiene (nbd).

Table 2. Cross-Coupling of Silanolate 4.

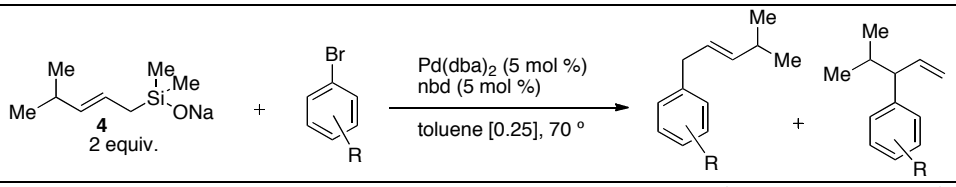


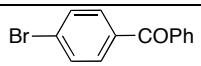
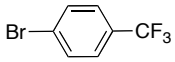
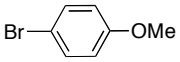
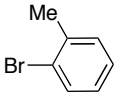
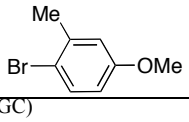
entry	Pd source	ligand (mol %)	yield,[a] (%)	ratio,[b] α:γ
1	$Pd(CF_3CO_2)_2$	 (20 mol %)	70	1:66
2	APC	 (20 mol %)	80	1:33
3	APC	 (20 mol %)	82	1:38
4	$Pd(dba)_2$	nbd (5 mol %)	82	1:32

a) Based on internal standard (biphenyl). b) Integrated area of the peaks (GC).

Fortunately, the conditions previously reported for the cross-coupling of allylic silanolate **1** cross-coupling were optimal when applied to γ-substituted allylic silanolate **4**. When *para*-substituted bromides were employed the selectivity of this coupling significantly decreased (Table 3). Electron deficient aryl bromides were observed to give high yields of the desired product with low γ-selectivity (Table 3 entries 1 and 2). Surprisingly, with an electron rich bromide, 4-bromoanisole, α-selective coupling occurred. Even more intriguing was that the selectivity was restored when *ortho*-substituted bromides were employed; clearly the steric environment about the palladium complex is of significant importance in determining the selectivity in these cross-coupling reactions.

Table 3. Survey of Aryl Bromides.

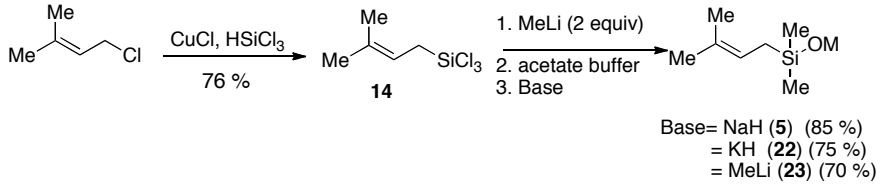


entry	bromide	product	conversion,[a] (%)	ratio,[a] α:γ
1		**9**	100	1:2
2		**10**	100	1:1.24
3		**11**	20	3.5:1
4		**12**	80	1:18
5		**13**	10	1:10

a) Ratio of integrated peaks (GC)

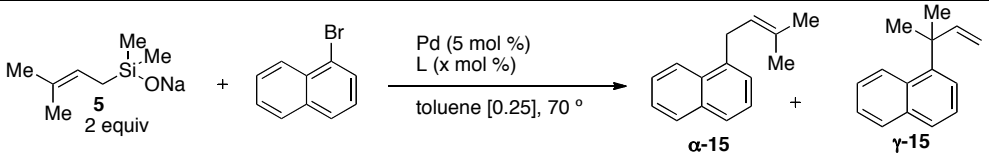
Ultimately, the scope was to be extended to γ-disubstituted allylic silanolates, specifically sodium dimethyl(3-methylbut-2-en-1-yl)silanolate, (**5**). The silanolate was synthesized by silylation of the commercially available prenyl chloride (Scheme 15). The trichlorosilane intermediate was then methylated, hydrolyzed in acetate buffer and deprotonated with sodium hydride to afford a white solid in good overall yield (85 %). Cross-coupling this substrate will afford achiral products containing a quaternary carbon atom. If the coupling reactions can be optimized to provide high selectivity and yields this method would then be applied to unsymmetrical γ-disubstituted allyl groups in order to provide chiral products containing quaternary carbon centers.

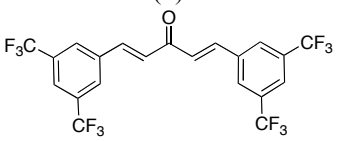
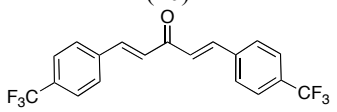
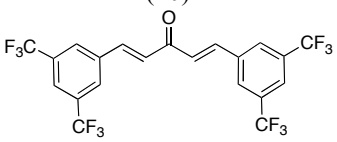
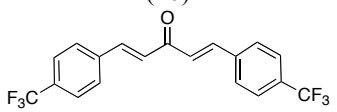
Scheme 15



Conditions were evaluated to discover the optimal catalyst and ligand conditions for the cross-coupling of prenyl silanolate **5** with 1-bromonaphthalene (Table 4). Applying the previous reaction conditions ($Pd(dba)_2$ and nbd) to this substrate led to high conversion but α-selective coupling was observed! By employing the electron deficient $Pd(CF_3CO_2)_2$ with dba-3,3',5,5'-CF_3, γ-selective coupling was obtained but with modest selectivity. Further manipulation of the palladium source and electron deficient ligand appeared to have little effect on the conversion and selectivity of the cross-coupling (Table 4, entries 3-5).

Table 4. Cross-Coupling of Silanolate 5.

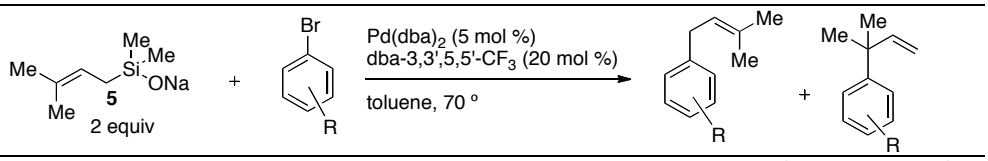


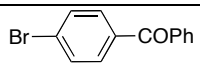
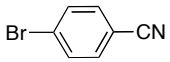
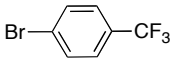
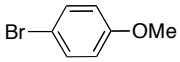
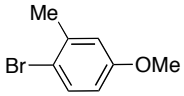
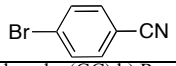
entry	palladium source	ligand (mol %)	conversion,[a] (%)	ratio,[a] α:γ
1	$Pd(dba)_2$	nbd (5)	98	1.3:1
2	$Pd(CF_3CO_2)_2$	 (20)	98	1:4.7
3	$Pd(CF_3CO_2)_2$	 (20)	88	1:3
4	$Pd(dba)_2$	 (20)	92	1:4.3
5	$Pd(dba)_2$	 (20)	83	1:5.7

a) Ratio of integrated peaks (GC).

The steric hindrance associated with 1-bromonaphthalene may negatively influence the γ-selectivity of the reaction; therefore, the reaction conditions were then applied to a variety of aryl bromides (Table 5). Surprisingly, the selectivities were poor for all the bromides tested. Interestingly, 4-bromobenzophenone was the only bromide that reacted completely. Other electron deficient aryl bromides stalled at moderate (4-bromobenzotrifluoride) and poor (4-bromobenzonitrile) conversions. Heating the reaction to higher temperatures slightly increased conversion at an expense of selectivity. For comparison to the previous silanolate tested, 4-bromo-3-methylanisole afforded low conversion and moderate γ-selectivity of the desired product. This result is contradictory to high γ-selectivity obtained when silanolate **1** was employed.

Table 5. Survey of Aryl Bromides.



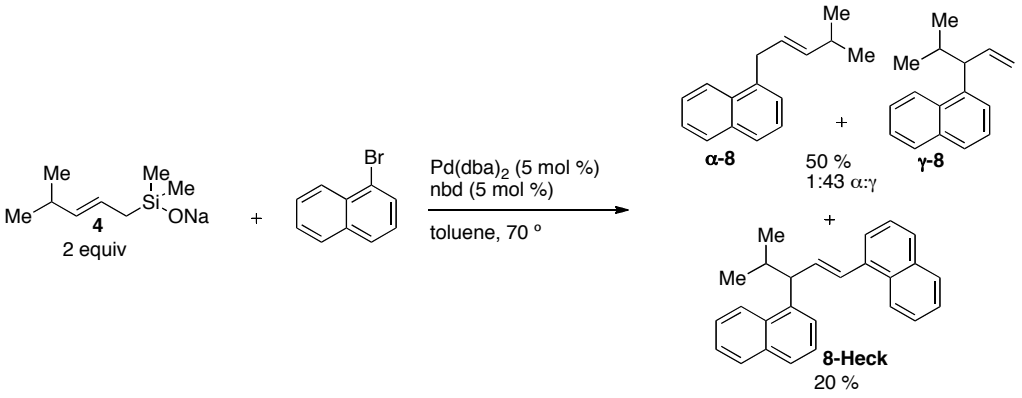
entry	bromide	product	time, h	conversion,[a] (%)	ratio,[a] α:γ
1		**16**	14 h	100	1:5.6
2		**17**	48 h	42	1:6
3		**18**	18 h	80	1:8
4		**19**	13 h	61	1:6
5		**20**	28 h	50	1:10
6[b]		**21**	13 h	65	1:7.6

a) Ratio of integrated peaks (GC) b) Reaction run at 90 ºC.

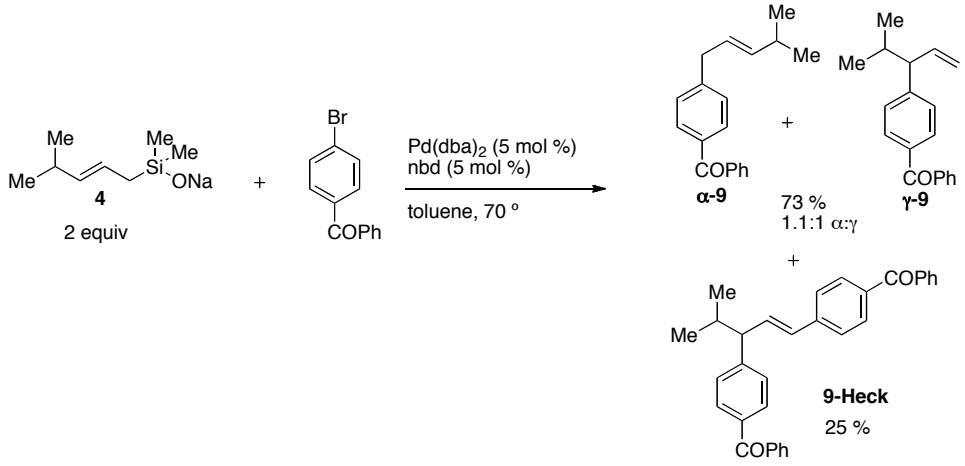
An important discovery was made during the isolation of the desired product. A major by-product in this reaction is a cinnamyl derivative arising from Heck-coupling of the aryl bromide with the terminal olefin of the branched *product*. Cross-coupling

silanolate **4** with 1-bromonaphthalene afforded moderate yields of the isolated products (50 %) with good γ-selectivity (1:43 α:γ). However, the Heck-coupled product was isolated in 20% yield (Scheme 16). No improvement was observed when the bromide employed was changed to 4-bromobenzophenone (Scheme 17).

Scheme 16



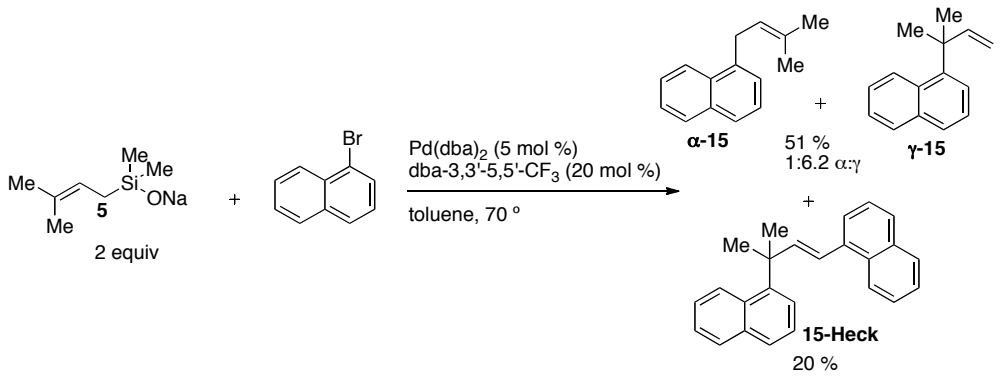
Scheme 17



Slightly higher yields of the desired product and Heck-coupled product were obtained. This side reaction was also prevalent in the cross-coupling of 1-bromonaphthalene with silanolate **5** (Scheme 18). It is readily apparent that this side reaction not only unproductively consumes the aryl bromide but also reacts with the

desired product *in situ* thus lowering the apparent selectivity of the cross-coupling reaction. This side product was isolated in lower yields; however, with the drastically lower selectivity observed with the *para*-substituted bromides it would be beneficial to discover conditions that effectively suppressed this side reaction.

Scheme 18



The similarities in yields of the Heck-product are particularly interesting because of the significantly lower selectivity observed when using silanolate **5**. This result suggests that another alternative pathway (besides the Heck-coupling) is leading to a decrease in the selectivity of the reaction.

3.3.2. Synthesis of Potassium and Lithium Silanolate Salts

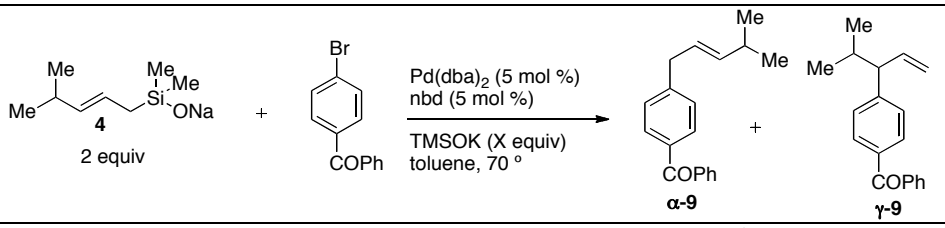
On the basis of the preliminary mechanistic model (Scheme 12) several intermediates can be shared between the desired cross-coupling pathway and Heck-coupling. The obvious intermediate is the aryl-palladium-halide complex; however, if transmetalation is the turnover-limiting step then the siloxy-palladium-aryl intermediate should be considered as a common intermediate. The silanolate is proposed to be a ligand to the palladium, which in turn inserts across the olefin. Hydride elimination

followed by hydrogen-oxygen reductive elimination affords the silanol species as well as palladium(0) to re-enter the catalytic cycle.

The initial hypothesis was to increase the rate of transmetalation, thereby decreasing the amount of unwanted Heck by-product. This hypothesis could be tested by: (1) adding a Lewis basic additive to facilitate transmetalation via anionic activation and (2) isolation and application of potassium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate, (**22**) as a more nucleophilic silanolate precursor. Increasing the nucleophilicity of the silanolate should facilitate anionic activation and thus the rate of transmetalation.[31] As a consequence, if the turnover-limiting step is displacement, changing to a more nucleophilic salt should also facilitate the reaction and lead to increased selectivity.

The most convenient variation to test was the addition of a basic additive. As previously described, the addition of a Brønsted base has found applications in cross-coupling reactions with silanols.[20b,23-24,25] Work from these laboratories has also revealed a beneficial effect of Lewis basic additives on the rate of cross-coupling with silanolate salts. In accordance with this theory, potassium trimethylsilanolate (TMSOK) was added to the cross-coupling reaction of **4** with 4-bromobenzophenone (Table 6). Surprisingly, the linear products were favored when TMSOK was used as an additive. Additionally, the rate of the reaction seemed to decrease significantly with larger loadings of TMSOK. While these initial results did not appear promising the isolation and application of a potassium silanolate salt was still warranted to gain a better understanding of the mechanism.

Table 6. TMSOK as Additive in Cross-Coupling.



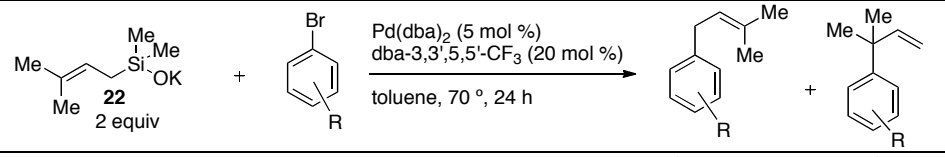
entry	TMSOK, (equiv)	time, (h)	conversion,[a] (%)	ratio,[a] α:γ
1	0.25	7	100	1.4:1
2	0.50	16	100	1.6:1
3	1.00	50	100	1.8:1

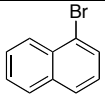
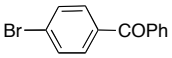
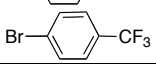
a) Ratio of integrated peaks (GC)

.

Potassium silanolate **22** was synthesized in a manner similar to **5** using KH in lieu of NaH in the final deprotonation step. The corresponding potassium silanolate salt was isolated as white solid in good yield (72 %). The salt was applied to the cross-coupling of different aryl bromides (Table 7). Unfortunately, using $Pd(dba)_2$ with dba-3,3',5,5'-CF_3 all of the reactions stalled at very low conversion and γ-selectivity. Sterically hindered bromides appeared to affect conversion (Table 7, entry 1) and α-selective coupling was observed for 4-bromobenzotrifluoride (Table 7, entry 3) .

Table 7. Cross-Coupling of Silanolate 22.



entry	aryl bromide	product	conversion,[a] (%)	ratio,[a] α:γ
1		**15**	10	1.6:1
2		**16**	20	1:6
3		**18**	25	2.2:1

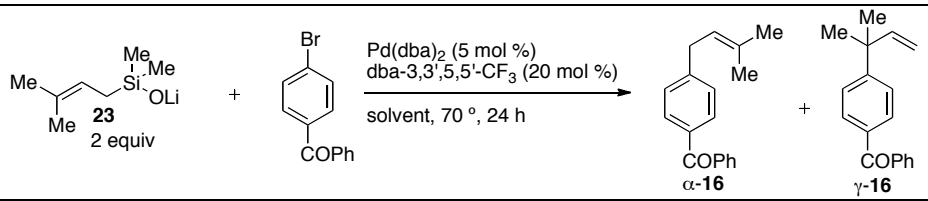
a) Ratio of integrated peaks (GC).

NMR spectroscopic experiments revealed the silanolate was reacting with the electron deficient olefin ligand. Despite the shortcomings of these experiments it was

learned that an activated pathway was detrimental to the selectivity and perhaps a less nucleophilic salt should be developed to prevent an activated pathway.

The lithium silanolate **23** was prepared using the same protocol as before, substituting MeLi for NaH or KH during the deprotonation procedure. This salt was isolated in high yields as a viscous oil and was applied to the cross-coupling with 4-bromobenzophenone. Using $Pd(dba)_2$ and dba-3,3',5,5'-CF_3 good γ-selectivity was obtained of the desired product (Table 8, entry 1). Not surprisingly, the rate of the cross-coupling was decreased and low conversion was observed after 24 h. In view of the increased selectivity obtained with this silanolate salt further investigation was warranted. The solvent was varied in the hope that a coordinating solvent would enhance the nucleophilicity of the silanolate enough to increase the rate of reaction and maintain the high selectivity observed with toluene (Table 8). When tetrahydrofuran (THF) and 1,2-dimethoxyethane (DME) were used as solvents, low conversion as well as γ-selectivity were observed. Dioxane proved to be the optimal solvent with complete conversion of the bromide and excellent γ:α selectivity observed at 100 ºC. Intriguingly, when the sodium silanolate was subject to the reaction conditions a complete reversal in selectivity was observed (Table 8, entry 6).

Table 8. Survey of Solvents.

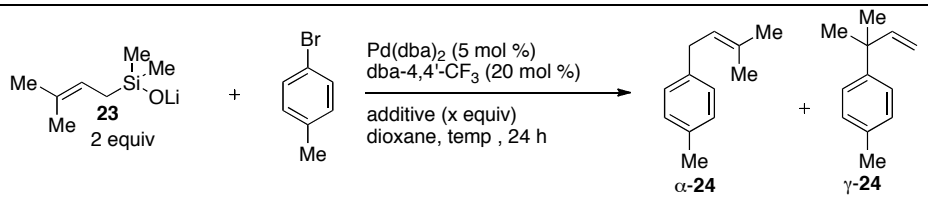


entry	silanolate	solvent	conversion,[a] (%)	ratio,[a] α:γ
1	**23**	toluene	10	1:20
2[b]	**23**	THF	25	1:9
3	**23**	DME	12	1:3.6
4	**23**	1,4-dioxane	45	1:26
5[c]	**23**	1,4-dioxane	100	1:33
6[c]	**5**	1,4-dioxane	97	62:1

a) Ratio of integrated peaks (GC). b) Reaction run at reflux. c) Reaction run at 100 ºC.

When these conditions were applied to 4-bromotoluene, incomplete conversion was observed. Additives were surveyed to determine if the Lewis basic carbonyl group in 4-bromobenzophenone had a beneficial role during cross-coupling (Table 9). Because of the Lewis basic carbonyl group present in 4-bromobenzophenone, benzophenone was the first additive tested. Unfortunately, low conversion of the desired product was obtained (25%). Other more Lewis basic solvents, THF, DME, and acetonitrile (MeCN) were employed. The first experiments were conducted with small amounts of the solvent; however, no significant increase in rate was observed (Table 9, entries 1-7). Increasing the amount of coordinating solvents had little effect on the amount of product obtained; even increasing the temperature to 120 ºC had little effect on the conversion (Table 9, entries 11-14).

Table 9. Survey of Additives in Dioxane.



entry	additive (equiv)	temp., (ºC)	conversion,[a] (%)	ratio,[a] α:γ
1	(1.0) benzophenone	100	25	1:12
2	(2.0) THF	100	30	1:35
3	(2.0) MeCN	100	26	1:44
4	(2.0) DME	100	32	1:39
5	(4.0) THF	100	32	1:57
6	(4.0) MeCN	100	26	1:22
7	(4.0) DME	100	30	1:28
8	(10.0) THF	100	31	1:11
9[b]	(4.0) THF	100	36	1:47
10[b]	(10.0) THF	100	37	1:33
11[b]	-	120	54	1:27
12[b]	(4.0) THF	120	30	1:17
13[b]	(10.0) THF	120	28	1:22
14[b]	(4.0) MeCN	120	58	1:20

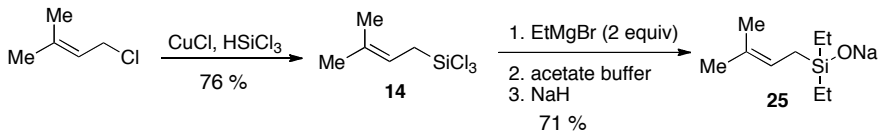
a) Ratio of integrated peaks (GC). b) Reactions performed in sealed tubes.

Despite the observed increase in γ-selectivity the lower nucleophilicity of the silanolate significantly lowered the rate of the cross-coupling. An alternative approach is needed to optimize the reactions conditions. Theoretically, slightly larger groups on the silicon should prevent activation at silicon during the transmetalation event and not affect the displacement step of the mechanism. It was proposed that by changing the dimethyl groups on silicon to ethyl groups, the activation mechanism will be disfavored and the displacement step should not be affected.

3.3.3. Preparation of Sodium Diethylsilanolate

Because of the fewer steps required to synthesize the prenyl silanolate derivative it was decided to prepare, test and optimize the diethylsilane version of this substrate as opposed to the synthetically cumbersome route to isopropyl substrate. Sodium diethyl(3-methylbut-2-en-1-yl)silanolate, (**25**) can be prepared from the starting chloride in a method analogous to the previous described syntheses. The intermediate prenyl trichlorosilane was treated with two equivalents of ethylmagnesium bromide to afford the triorganochlorosilane which was hydrolyzed *in situ* to provide the silanol which was purified by column chromatography. On the basis of previous observations that allylic silanols are unstable to isolation, the silanol was kept in solution and used immediately in the deprotonation step with sodium hydride. The silanolate salt was obtained as a white solid in 71% yield after three steps (Scheme 19). Alternatively, the silanolate can me prepared by treating the prenyl chloride with magnesium turnings and trapping the Grignard reagent with diethyldichlorosilane. However, a mixture of products containing terminal and internal olefins were formed due to the instability of the prenyl Grignard reagent. The silanolate was formed from this method in lower yields than the aforementioned route and with a slight isomeric mixture. Accordingly, the synthesis of the silanolate should be performed employing the trichlorosilane procedure.

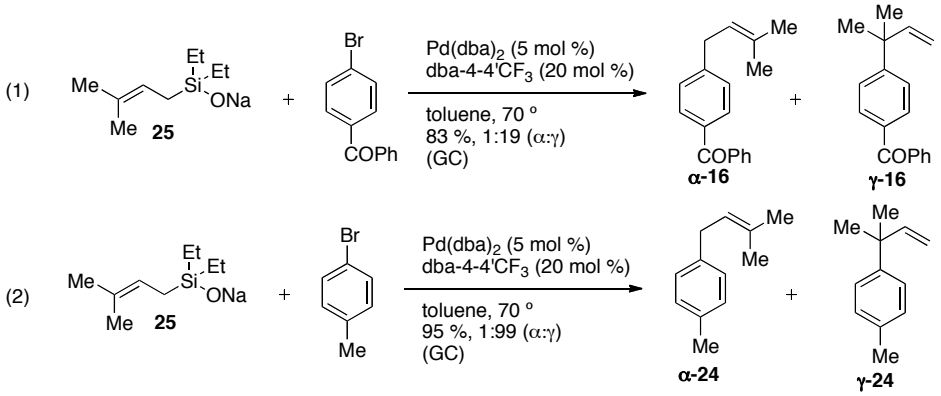
Scheme 19



The silanolate was applied in a series of cross-coupling experiments and the selectivity of the desired product was measured. Using $Pd(dba)_2$ and dba-4-4'-CF_3, the

cross-coupling with 4-bromotoluene or 4-bromobenzophenone, excellent γ-selectivity was observed for the desired products (Scheme 20). These preliminary experiments demonstrated that the more hindered diethyl silanolate significantly increased the α:γ selectivity of the cross-coupling reaction. Further optimization was needed to ensure complete consumption of the bromide and to also ensure the high selectivity is maintained in the cross-coupling reaction.

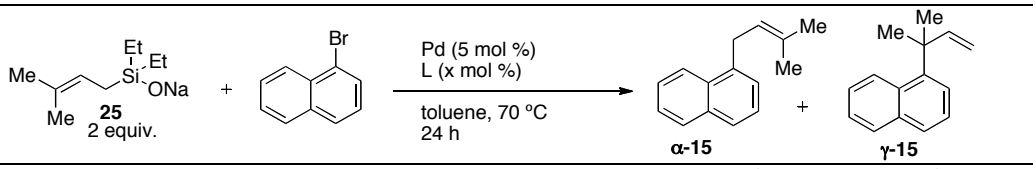
Scheme 20



The incomplete consumption of the aryl bromide observed with the reaction conditions described above prompted a ligand survey to drive the reaction to completion. Employing triphenylphosphine and tri(2-furyl)phosphine as ligands resulted in low selectivity of the desired product (Table 10 entries 1 and 2). However, employing tri(pentafluorophenyl)phosphine resulted in excellent γ-selectivity in poor conversions (Table 10, entry 4). No reaction was observed when tricyclohexylphosphine was employed as a ligand (Table 10, entry 7). Triphenylarsine was tested as it has been shown to have a beneficial influence on the rate of coupling in Stille reactions.[37] However, low reactivity was observed when applying this ligand to this cross-coupling procedure (Table 10, entry 3). The previous optimal ligand, nbd, was also tested to afford

high conversion and low selectivity of the products (Table 10, entry 6). It was concluded that the olefin ligand, dba-4-4'-CF_3, provided the product in the highest conversions (100) and γ-selectivity (1:20, α:γ) for the cross-coupling with 1-bromonaphthalene.

Table 10. Survey of Ligands.



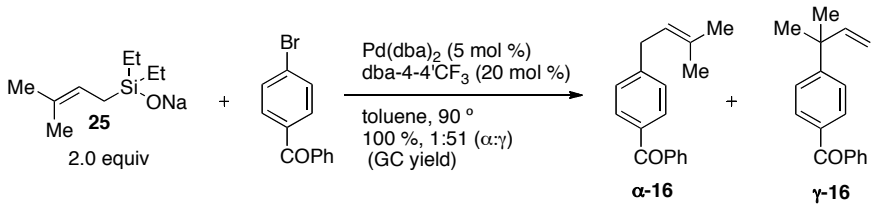
entry	Pd source	ligand, (mol %)	conversion.[a] (%)	ratio,[a] α:γ
1	$Pd(dba)_2$	(10) Ph_3P	60	1:3.3
2	$Pd(dba)_2$	(10) tri(2-furyl)phosphine	100	1:2.3
3	$Pd(dba)_2$	(10) Ph_3As	21	1:10
4	$Pd(dba)_2$	(20) dba-4-4'-CF_3	100	1:20
5	$Pd(dba)_2$	(10) $(C_6F_5)_3P$	< 5	1:22
6	$Pd(dba)_2$	(5) nbd	100	1:4
7	$Pd(OAc)_2$	(20) Cy_3P	0	NA

a) Ratio of integrated peaks (GC).

The optimized conditions for 1-bromonaphthalene led to incomplete conversion when 4-bromobenzophenone was employed. It was envisaged that the potassium silanolate might enhance the reaction rate if the turnover-limiting step was displacement of the silanolate on the arylpalladium halide complex. The synthesis of the potassium salt was carried out and applied to the reaction conditions. Unfortunately, this silanolate was unstable to the reaction conditions and no reaction was observed. Gratifyingly, raising the temperature of the reaction to 90 ºC when using the electron-deficient aryl bromides allowed complete consumption of the starting material (Scheme 21). The amounts of silanolate and ligand added were also surveyed with little effect on the rate of

the reaction; however, 0.2 equivalents of olefin ligand were required to obtain high selectivity of *ortho*-substituted bromides.

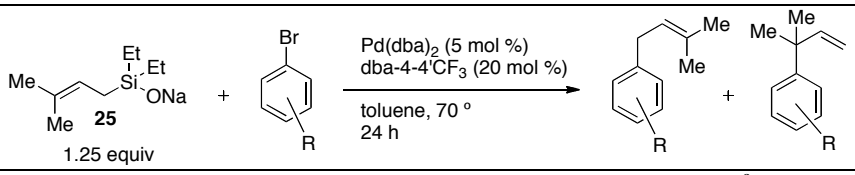
Scheme 21

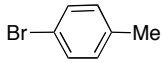
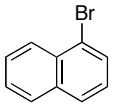
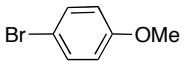
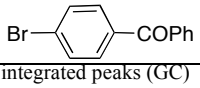


3.3.4. Heck-coupled Product and Final Optimizations

Having optimized the preliminary coupling conditions with silanolate salt **25**, scale-up/isolation experiments were conducted (Table 11). Higher yields were obtained when 4-bromotoluene (Table 11, entry 1) and 1-bromonaphthalene (Table 11, entry 2) were employed as the aryl bromides. Slightly lower selectivities were obtained for hindered and electron deficient bromides (Table 11, entries 2 and 4). Lower yields were obtained for 4-bromoanisole (Table 11, entry 3), presumably due to increased yield of the Heck-byproduct (25%). Unforeseen by previous analysis methods, significant amounts of the Heck-coupled product were isolated from the cross-coupling reactions. This result was surprising considering the excellent γ:α selectivity observed with these cross-coupling reactions. Additionally, the bromides with the lowest selectivity (1-bromonaphthalene and 4-bromobenzophenone) led the *least* amount of Heck coupled product. The discovery that the Heck-coupling pathway is still operative with the diethyl silanolate warranted further investigation.

Table 11. Preparative Cross-Coupling of Silanolate 25.

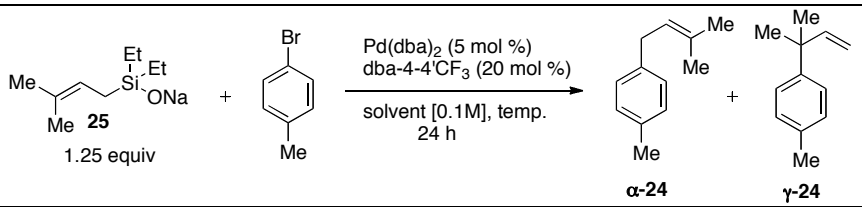


entry	bromide	product	yield, (%)[a] (heck, (%))	ratio,[b] α:γ
1		**24**	70 (20)	1:99
2		**15**	75 (15)	1:54
3		**19**	57 (25)	1:99
4		**16**	65 (15)	1:50

a) Isolated yield. b) Ratio of integrated peaks (GC)

It was proposed that running the reaction at lower concentrations would limit the Heck coupling since the transmetalation step is an intramolecular process while the undesired Heck-coupling is intermolecular. However, at lower concentrations the reaction did not go to completion and it is postulated that displacement is the rate-limiting step. Coordinating solvents may accelerate the displacement step at low concentrations to provide high yields of the desired product and prevent Heck coupling from occurring. Screening a variety of different solvents at low concentrations provided limited results (Table 12). Comparable to the previous survey, DME and THF afforded the desired product in poor yields and low γ-selectivity. Dioxane maintained the high γ-selectivity; however, complete consumption of the bromide was not observed using this solvent. Acetonitrile and DMF led to a minimal amount of cross-coupling and it is probable that the silanolate is not stable under these conditions. With limited alternatives remaining a more in-depth survey of ligands was needed; however, unlike the previous surveys, analysis conditions have been developed to better monitor the formation of the Heck by-product and a suitable ligand can be selected on the basis of this analysis.

Table 12. Survey of Solvents.

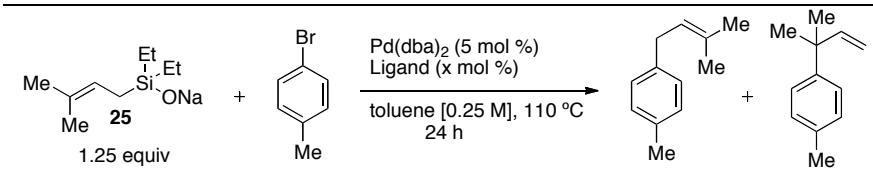


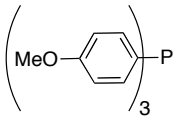
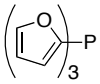
entry	solvent	temp, (° C)	SM remaining,[a] (%)	yield,[a] (%) (heck, (%))	ratio,[b] α:γ
1	DME	85	32	35 (10)	1:2
2	THF	67	27	45 (12)	1:5
3	1,4-dioxane	100	0	65 (25)	1:30
4	MeCN	81	80	< 10	99:1
5	DMF	110	15	0	NA

a) Based on GC analysis using biphenyl as internal standard. b) GC analysis using ratio of peak areas.

Employing electron rich phosphine ligands (Cy_3P and t-Bu_3P) complete γ-selectivity was observed; however, very little conversion to the desired product was seen. Ligands S-Phos,[38] X-Phos,[39] and RuPhos[40] were also tested as potential ligands with very limited reactivity. More conversion was obtained with tri(4-methoxyphenyl)phosphine; however, larger amounts of the Heck-coupled product were observed (Table 13, entry 8). Trialkyl- and triphenylphosphite ligands gave excellent γ-selectivity; however, moderate yields of the desired product and large amounts of Heck product were obtained (entries 9-11). Lower yields of Heck-coupling was observed with triphenylphosphine and tri(2-furyl)phosphine but the products were obtained in poor yields. Triphenylarsine and triphenylantimony were also tested as potential ligands. Initial results with these ligands seemed promising as the amount of Heck coupling produced with these conditions decreased (Table 13). However, these ligands were not without their own set of complications.

Table 13. Survey of Ligands.



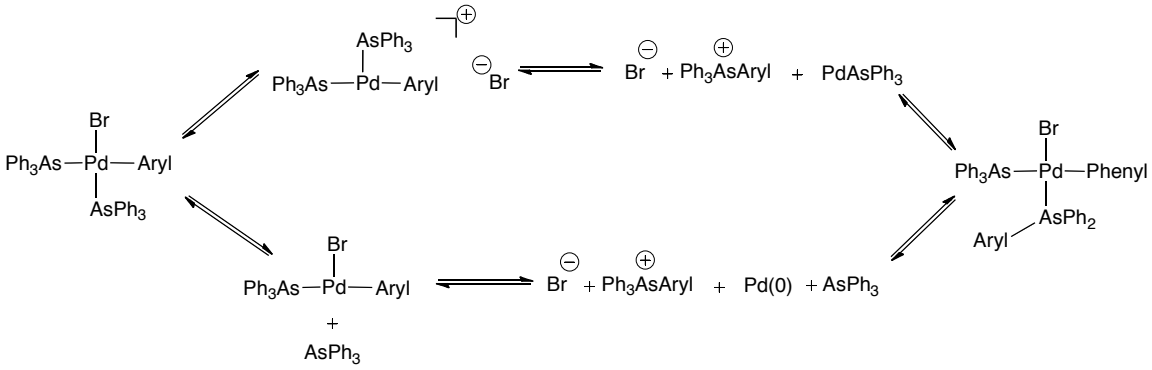
entry	ligand, (mol %)	SM remaining,[a] (%)	yield,[a] (%) (heck, (%))	ratio,[b] α:γ
1	(5) Cy_3P,	40	20 (5)	only γ
2	(5) $(t\text{-Bu})_3P$	5	5 (0)	only γ
3	(5) S-Phos	53	5 (0)	3:1
4	(5) X-Phos	5	50 (13)	1:11
5	(5) RuPhos	50	10 (5)	1:1
6	(10) 	5	65 (20)	1:65
7	(10) Ph_3P	15	25 (7)	1:31
8	(10) 	5	15 (5)	1:30
9	(10) $(OMe)_3P$	16	50 (20)	1:99
10	(10) $(OEt)_3P$	9	50 (18)	1:99
11	(10) $(OPh)_3P$	31	30 (26)	1:90
12	(10) Ph_3As	4	60 (7)	1:99
13[c]	(10) Ph_3As	13	60 (6)	1:46
14[c]	(10) Ph_3Sb	0	40 (10)	1:99
15	(10) $(C_6F_5)_3P$	51	20 (5)	only γ
16	(5) dppe(O)	15	40 (12)	1:99
17	(5) dppp(O)	20	35 (22)	1:99

a) Based on GC analysis using biphenyl as internal standard. b) GC analysis using ratio of peak areas.

c) Reaction performed using APC (2.5 mol %) in lieu of $Pd(dba)_2$

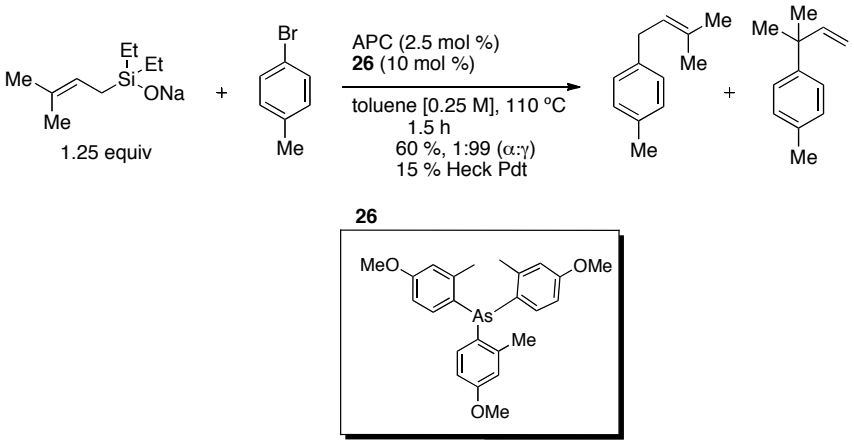
Isolation of the products from these experiments revealed another by-product was formed when triphenylarsine or triphenylantimony was used as the ligand. Aryl exchange from the arsine ligand to the palladium center was occurring and an inseparable product was formed as a consequence of this transfer (Scheme 22).[41]

Scheme 22



A more sterically encumbered arsine ligand, tris(4-methoxy-2-methylphenyl)arsine (**26**), was employed under the coupling conditions to prevent the aryl transfer from occurring.[42] This type of exchange was indeed prevented; however, the amount of Heck coupling observed in these reactions increased to previous levels. It is proposed that more ligand manipulation and evaluation is needed to limit the Heck coupling and provide high yields of the desired branched products.

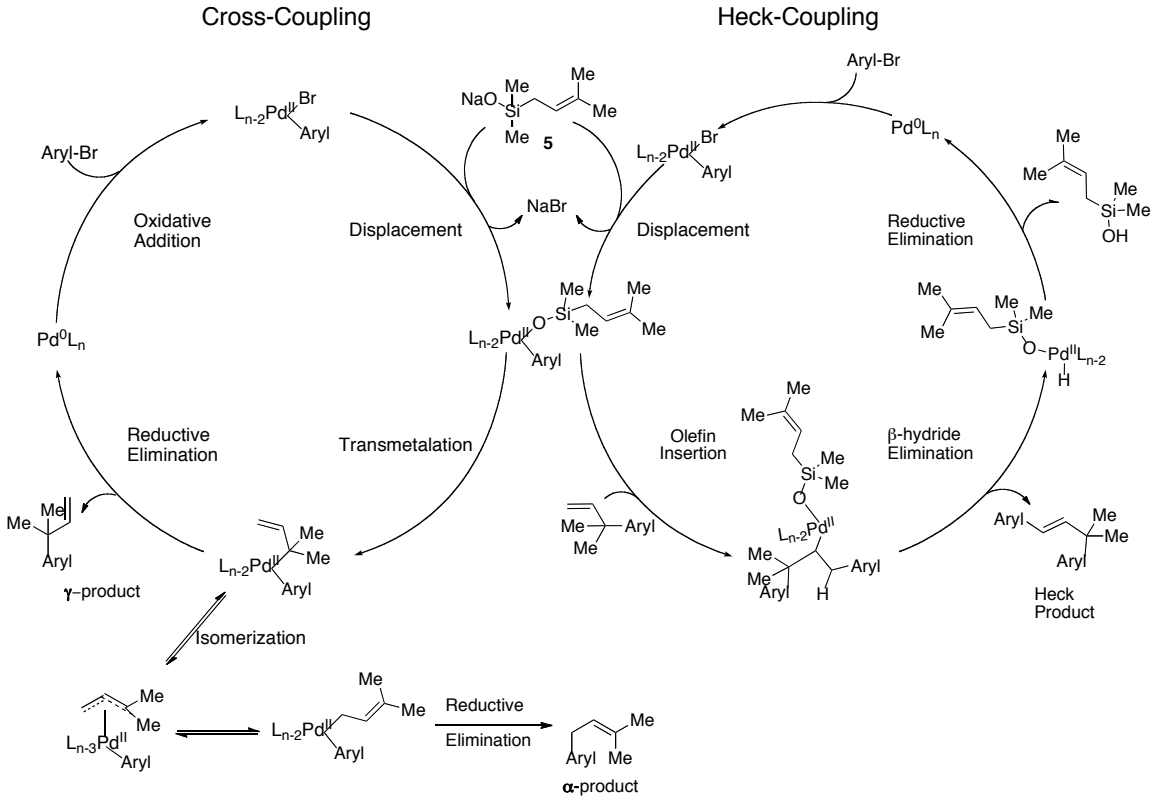
Scheme 23



3.4. Discussion

The selective cross-coupling of γ-substituted allylic silanolates proved to be a challenging endeavor. Following the initial mechanistic understanding it was presumed that the major challenge to controlling the selectivity was by increasing the rate of reductive elimination and preventing the π-allyl isomerization of the intermediate palladium complex (Scheme 12). However, from the initial results employing the dimethylsilanolates, Heck-coupling with the desired product may be severely limiting the apparent selectivity of the reactions (Scheme 16-18). On the basis of this data, a new mechanistic picture has been formulated incorporating this alternative pathway (Scheme 24).

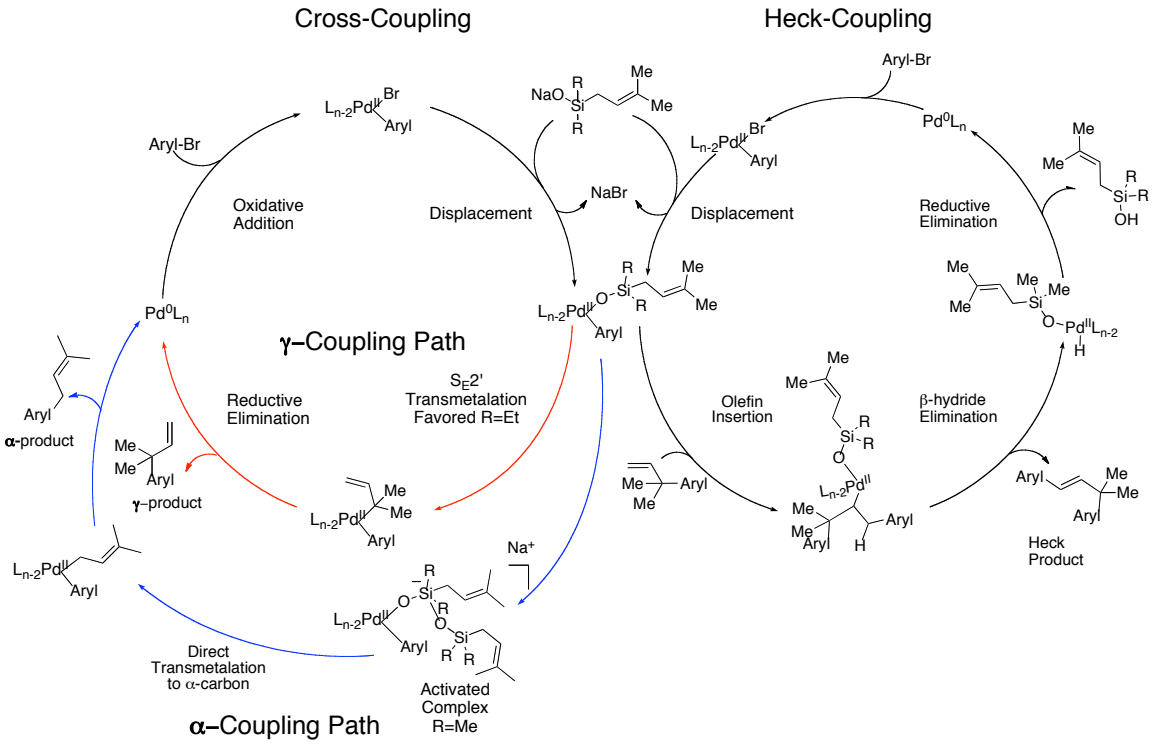
Scheme 24



Further experimentation employing a more nucleophilic silanolate provided limited amount of data for the mechanistic picture; however, by lowering the nucleophilicity and/or by preventing anionic activation at silicon by the use of bulky, silyl groups, the γ-selectivity significantly increased (Table 8 and Table 11). This discovery is paramount for the elucidation of the mechanism. Clearly, it is detrimental for the transmetalation to undergo an activated pathway. The discovery that the Heck coupled product is still observed (with high γ-selectivity) without anionic activation demonstrates that the Heck pathway is only a minor contributor to the selectivity observed with this reaction. The highest selectivities were obtained with the less nucleophilic lithium silanolate or the diethylsilanolate. The high selectivity was maintained even in the absence of electron deficient olefins, which were previously thought to be critical for

high γ-selectivity. From this new data a clearer mechanistic pathway can be formulated in which the anionic activation pathway could give rise to an enhanced rate for direct α-transmetalation (Scheme 25).

Scheme 25



The γ-selectivity significantly increased by using the diethylsilanolate **25** despite the consistency of the yield of the Heck-product (compare Table 5 with Table 11). Thus, π-allyl isomerization is not contributing (or occurring) to the overall selectivity since this step would be independent of the silanolate employed. The high selectivity, as a function of silanolate, can only be manifested in intermediates in which the silanolate species is present (displacement or transmetalation). A preliminary hypothesis is that the α:γ selectivity is a consequence of the type of transmetalation occurring. When smaller alkyl groups on the silane are employed and anionic activation can occur giving rise to direct

α-transmetalation; however, if this activation cannot occur then S_E2' transmetalation occurs preferentially leading to the γ-coupled product. This theory can also explain why good γ-selectivity was only obtained in the cross-coupling of the sodium silanolate **4** with hindered bromides. The steric interactions arising from *ortho*-substituent could prevent activation at silicon and lead to a γ-selective process. More mechanistic work is needed to verify this theory. While this work cannot explicitly rule out that displacement is the turnover-limiting step, it can be assumed that for unhindered bromides the *selectivity*-determining step is occurring during transmetalation.

The greatest challenging that needs to be overcome in this reaction is that of the Heck-coupling. The initial problem of selectivity was addressed and solved with the use of silanolate **25**; however, the problem of Heck coupling is still very prominent. From the current mechanistic understanding it is possible that multiple intermediates are shared between the two coupling reactions and conditions must be developed to favor the desired allylic coupling over the Heck coupling. Subtle effects have been observed to lower the yield of the Heck-coupled products. An optimal concentration range is associated with the cross-coupling reaction. Concentrations above 0.5 M increased the yield of the Heck reaction. Conversely, concentrations lower than 0.1 M were observed to significantly slow the rate of reaction. This trend can be explained on the basis of bimolecular collisions. Under high concentrations the turnover-limiting step is, most likely, transmetalation since the rate of displacement *via* a bimolecular process is facile due to a higher probability of interactions. However, at higher concentrations the rate of Heck coupling accelerates due to this same effect. As the reaction progresses the effective concentration of product increases relative to the silanolate, which can lead to

the Heck reaction occurring faster than the desired coupling. In contrast, at low concentrations the displacement step can be considered to be rate limiting due to the lower probability of the bimolecular collisions between the aryl-Pd-Br complex and the silanolate. The immediate product of oxidative addition is certainly competent in both pathways and if the displacement step is slow at high dilution, then the Heck reaction will also be competing with the desired allylic cross-coupling.

Temperature and ligands were also observed to have beneficial effects on the rate of cross-coupling with respect to the Heck-coupling. Raising the temperature to refluxing toluene improved the yields of the desired product and decreased the yields of the Heck coupled product. This can be explained due to a slow rate of transmetalation to a trisubstituted sp^2-carbon. By adding more energy into the system the rate of transmetalation was increased with respect to the rate of the Heck reaction. It was discerned that a subtle ligand effect on the outcome of the reaction. While no clear trend can be discerned, it can be predicted that a ligand is needed that is able to facilitate oxidative addition to an aryl bromide while still providing enough Lewis acidity to induce an electrophilic palladium(II) intermediate to facilitate transmetalation. As reported above, synthesis of arsine derivatives or exploring alternative phosphine sources (further bidentate ligands, bppbO, phosphine oxides) may provide the optimal electronic environment to enhance the rate of transmetalation.

3.5. Conclusions and Outlook

The cross-coupling of γ-substituted allylic silanolates proved to be a more difficult endeavor than originally proposed. Despite several challenging hurdles throughout the course of the project, a large amount of information and mechanistic

elucidation was obtained. The original mechanism, while not flawed, failed to reveal all of the competing pathways associated with this type of coupling reaction. The development and application of the diethylsilanolate salt **25** proved to be very effective at maintaining high γ-selective coupling with aryl bromides. As a consequence, chiral phosphine ligands can be employed toward catalytic enantioselective cross-coupling. A ligand type previously thought to be incompatible with this class of silanolates due to the poor selectivity associated with the sodium dimethylsilanolates **4** and **5**.

The major hurdle that is apparent to this reaction is limiting the amount of the Heck coupling. As discussed above, synthesis of ligands with varying electronic influences toward palladium is a likely solution to this problem. The optimization of this reaction has progressed nicely throughout this project and only one major hurdle remains to be addressed. The synthetic utility of this reaction will be readily apparent once optimal conditions are discovered to obtain high yields and selectivities. While the isopropyl substrate was originally synthesized and tested, a more intriguing class of substrates would be unsymmetrical γ-disubstituted allylic silanolates (Figure 3). This class of substrates will afford products that are not only chiral but contain a quaternary carbon as its chiral center. This class of chiral compounds has proven to be of great synthetic challenge and a novel cross-coupling route to these products would be of significant impact.[43]

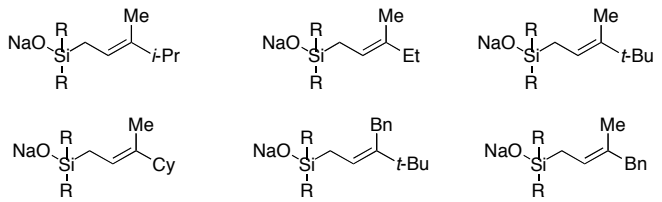


Figure 3. Unsymmetrical γ-disubstituted silanolates.

Cinnamyl silanolates represent another class of compounds that should be considered after optimal conditions are discovered. Preliminary experiments using this class of substrates were not promising, giving rise to α-selective couplings. Metallocinnamyl nucleophiles have been reported in very few classes of γ-selective cross-coupling reactions, presumably due to the instability of the deconjugated olefin. However, cinnamyl trifluoroborates have been reported to couple selectively at the γ-position.[9c] Upon further optimization of the allylic silanolate coupling, the conditions should be applied to this class of substrates in order to determine if this rare class of organodonor can be coupled selectively at the γ-carbon.

Chapter 4. Development of a Differentiated 1,2-Bissilylethene Reagent

4.1. Introduction

Polyenes and stilbenes represent an important class of organic compounds due to their prevalence in the polymer and fine chemical industry.[44] Recently, natural products containing large macrocyclic polyenes have been the focus of many total syntheses due to the ability of the compound to act as ion channels in biological systems.[45] The most common method to prepare these compounds focuses on transition metal catalysis, specifically, olefin metathesis, sp^2-sp^2 cross-coupling, and Heck reactions.[46] Olefin metathesis is a very common approach to close macrocylces; however, this method is best conducted with terminal olefins and chemoselectivity may suffer when multiple alkenes are present within the molecule.[47]

The Heck coupling presents a very classical disconnect in organic synthesis; however, inherent problems are associated with this reaction. Problems arise in controlling the geometry of the olefin product as well as mixtures of 1,1- and 1,2-disubstituted olefins are obtained from the reaction.

Alkene-sp^2 cross-coupling has emerged as a prominent method to synthesize polyenes and stilbenes due to the functional group compatibility of the reactions. Additionally, the cross-coupling employs a large class of organonucleophiles including: alkenyl-stannane (Stille), -boronic acids/esters(Suzuki), -zinc (Negishi), and -silanes (Hiyama-Denmark).[3] Considering the utility of cross-coupling reactions it would be advantageous to incorporate multiple sites of reactivity to streamline syntheses of

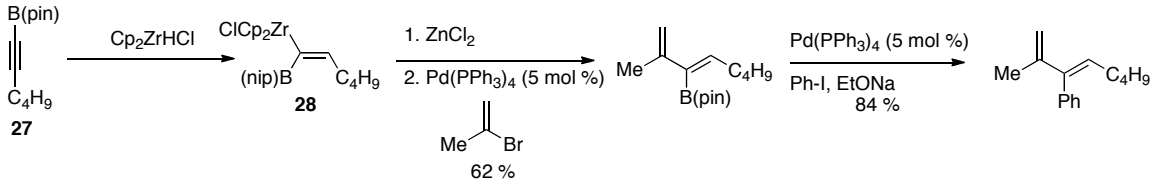
complex molecules. To access unsymmetrical polyenes and stilbenes a bifunctionalized olefin unit, exploiting the difference in reactivity between metal surrogates and provide an expedient route to complex olefin products.

4.2. Background

4.2.1. Bismetallic Reagents

Mixed-metal alkenyl reagents have been prepared that take advantage of the difference in reactivity between boron-zinc[48], boron-zirconium[49], boron-tin[50], zinc-tin[51], silicon-tin[52], and silicon-boron[53] reagents. The geminal mixed-metal reagents are typically generated by reduction of a borylated alkyne followed by trapping with the appropriate metal species. Hydrozirconation of 2-(hex-1-yn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, (**27**) affords the 1,1-mixed metal hexene derivative, **28**. The reactivity differences between boron and zirconium allow iterative cross-coupling to be conducted to afford the functionalized diene product (Scheme 26).[54]

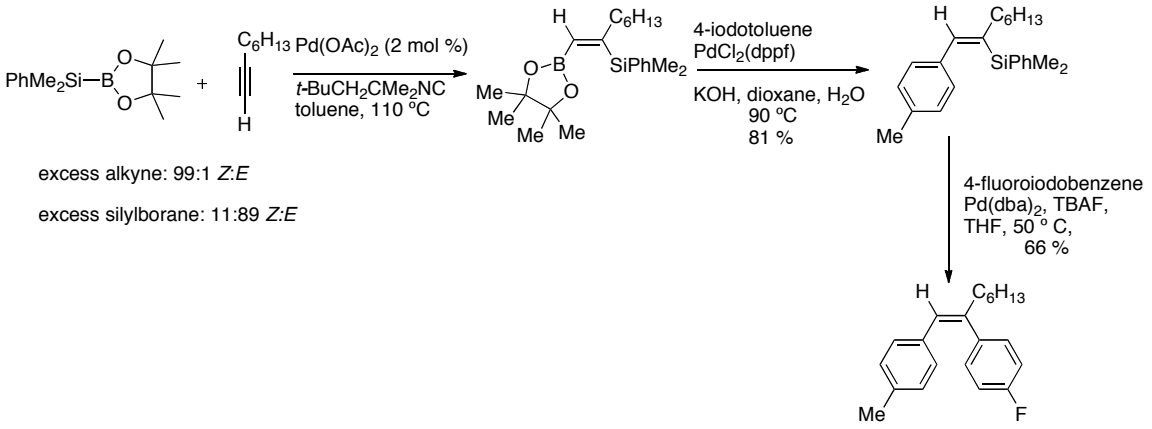
Scheme 26



1,2-Mixed metal species have been prepared by transition metal catalyzed addition of a metal-metal substrate across an alkyne. Typically, these reagents are prepared using silylboranes which adds both metals stereo-specifically to afford the *cis*-bismetallene adduct (Scheme 27).[53a,53c] The *trans*-adduct can be favored by using excess

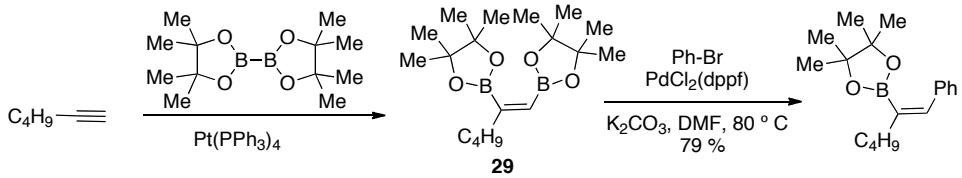
of the silylborane reagent. The 1,2-silylborene compound is used in sequential Suzuki/Hiyama couplings to afford *cis*- and *trans*-stilbene derivatives. The benefit of using mixed-metal alkenes is manifested in the different conditions required to conduct the cross-coupling with aryl halides.

Scheme 27



Bismetallic alkenes incorporating the same metal across the olefin have been prepared and utilized but to conduct iterative couplings steric and/or electronic perturbations must be present. 1,1- and 1,2-Bisboryl alkenes have been synthesized and utilized in sequential cross-coupling sequences. Unlike the mixed metal reagents these substrates are only selective because of the difference in steric environments about each boron center (Scheme 28).[55] (*E*)-2,2'-(Hex-1-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane), (**29**) is prepared by the addition of bis(pinacolato)diboron across 1-hexyne. The less hindered, terminal boryl group reacts preferentially during the cross-coupling with bromobenzene. The exploitation of different steric environments has also been observed in the selective cross-coupling 1,1-bisstannyl alkenes.[56] The reliance of steric differentiation is a severe limitation in the synthesis of complex molecules as the required steric environments may not be present during synthesis.

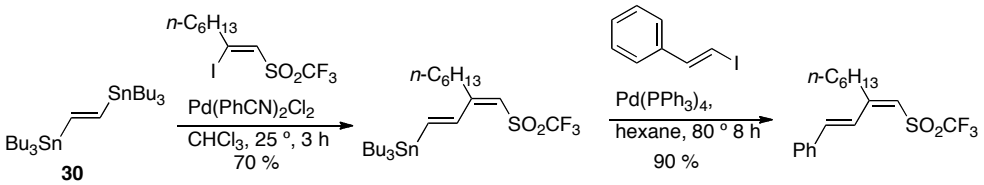
Scheme 28



4.2.2. 1,2-Bismetalloethene

The methods described thus far have utilized bismetallic-functionalized alkene derivatives which allows facile synthesis of complex molecules containing multiple sites of unsaturation. However, it would be highly beneficial to utilize this type of differentiation employing bismetalloethene units. The potential to install this unit as a lynchpin reagent, incorporating the ability to functionalize the terminal end, presents an attractive method to synthesize polyene, styrene, and stilbene derivatives. Despite this need, few 1,2-bismetalloethene units have been prepared *and* utilized in sequential cross-coupling methodology. *E*-1,2-bis(tributylstannyl)ethylene, (**30**) is the most commonly used substrate in this class of compounds.[56] Major limitations are associated with this compound including the extrusion of stoichiometric amounts of toxic tin by-products. Another major limitation is that the sequential coupling procedure must first employ an electron deficient halide in order to deactivate the second coupling and allow the reaction to be selective (Scheme 29). This drawback severely limits the scope of the reaction and novel methods should be developed in order to circumvent this problem.

Scheme 29

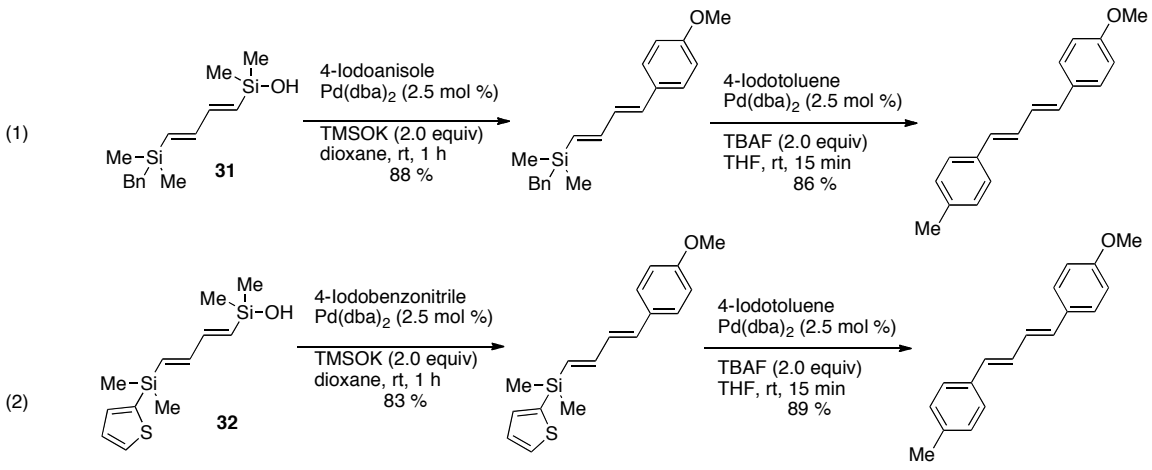


1,2-Bisboryl ethene and 1-tributylstannyl-2-ethenyl MIDA boronate units have been prepared recently;[57] however, neither of these reagents were applied to sequential cross-coupling protocols. Due to the lack of literature precedent to incorporate an unsubstituted bismetalloethene unit that is easily prepared, non-toxic, and can be readily discriminated between the two sites of reactivity, it is believe that a 1,2-bissilylethene unit can be utilized to fulfill this synthetic shortcoming.

4.2.3. Differentiated 1,2-Bissilylethene Unit

Organosilicon compounds present a rare opportunity in cross-coupling reactions in which two modes of action can be applied to induce cross-coupling: (1) the fluoride promoted pathway utilizing alkyl-,[15] alkoxy-,[11,16] and/or fluorosilanes[15] and (2) fluoride-free coupling utilizing organosilanols and silanolates.[23-25,28,30] By exploiting these two modes of activation sequential fluoride-free and fluoride promoted cross-coupling reaction could be employed on molecules bearing two different silyl moieties. Previous experiments performed in these laboratories demonstrated that compounds containing differentiated silyl groups can undergo fluoride-free coupling selectively followed by fluoride promoted coupling to provide unsymmetrical products (Scheme 30).[58]

Scheme 30

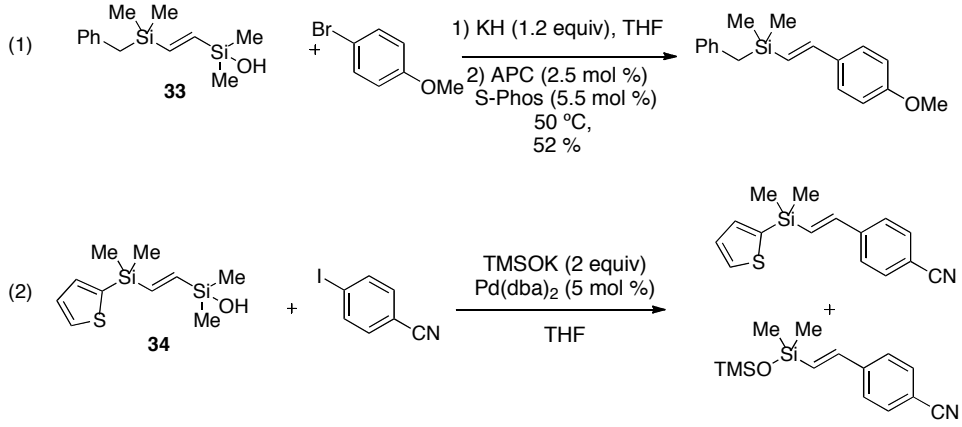


In the coupling of ((1*E*,3*E*)-4-(benzyldimethylsilyl)buta-1,3-dien-1-yl)dimethylsilanol, (**31**) the benzyl group would undergo migration during the fluoride promoted coupling if electron poor iodides were employed during the first cross-coupling. This problem was circumvented by changing the benzyl moiety about the distal silane to a 2-thienyl group, **32**. The 2-thienyl group led to increased rate of the desired coupling and iterative cross-coupling could be conducted with electron deficient halides.

The use of fluoride-free conditions followed by fluoride activated coupling presents an interesting approach for the coupling of a 1,2-differentiated ethene unit. Employing the same method used in the 1,4-sequential coupling process preliminary experiments from these laboratories employed two different 1,2-bissilylethene units for the tandem cross-coupling with aryl iodides (Scheme 31). Unfortunately, both were met with stability issues under the reaction conditions. Employing (*E*)-(2-(benzyldimethylsilyl)vinyl)dimethylsilanol, (**33)** as a differentiated reagent worked well in the cross-coupling of electron rich aryl halides. However, similar to previous reports

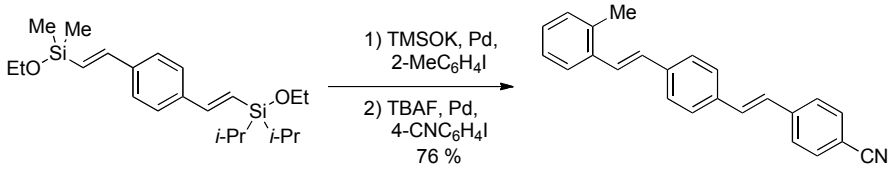
electron deficient intermediates were prone to undergo benzyl migration during fluoride coupling conditions.[58] Employing (*E*)-(2-(dimethyl(thiophen-2-yl)silyl)vinyl)dimethylsilanol, (**34**) to circumvent this problem, the 2-thienyl group was observed to cleave and form a mixed disiloxane species when TMSOK was used as a basic additive. Together, both reagents would provide a synthetic route to numerous polyene and stilbene derivatives; however, the requirement of two different coupling precursors precludes this method from being practical.

Scheme 31



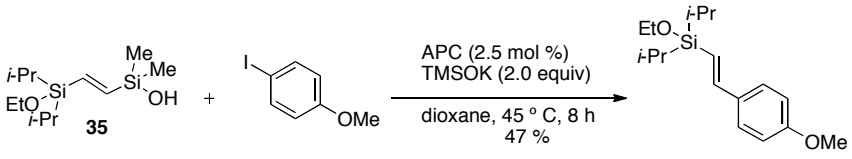
Because of the problems inherent with the previously prepared 1,2-bissilylethene units, another type of organosilane compound needed to be considered that was stable to basic conditions. Prior studies in this group examined the stability and rate of cross-coupling of alkoxysilane derivatives in the presence of basic additives.[59]

Scheme 32



The observation that diisopropyl ethoxysilane was stable during basic cross-coupling conditions and showed no rate decrease during fluoride promoted coupling posed as an excellent starting point toward the application of a 1,2-bissilylethene moiety. It should be noted that previous group members briefly studied (*E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol, (**35**) in a sequential cross-coupling protocol. After surveying numerous conditions, the cross-coupling of **35** with 4-iodoanisole resulted in low yields (<50 %) of the desired product (Scheme 33). The reaction suffered from prolonged times to completion, isomerization of the olefin, and reduction of the iodide. Attempts at coupling **35** employed TMSOK as the basic additive and the silanolate was never prepared stoichiometrically. The shortcomings of the cross-coupling with reagent **35**, may have been a result of using a basic additive during the cross-coupling. By forming the silanolate prior to the coupling conditions the need for a basic additive may be alleviated. It was the goal of this research to investigate this substrate further by stoichiometrically forming the silanolate prior to cross-coupling.

Scheme 33



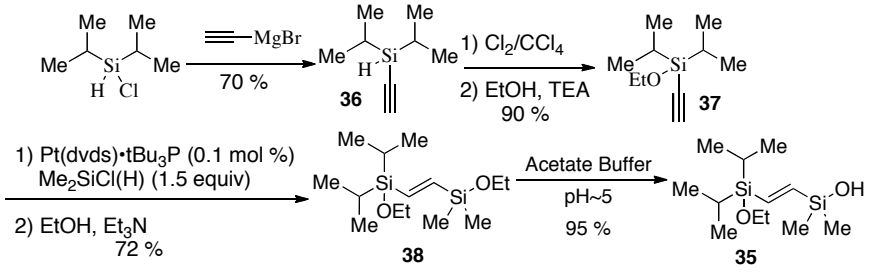
4.3. Results

4.3.1. Preparation of 1,2-Bisilylethene Reagent

The synthetic approach to **35** was carefully considered and after much optimization a six-step procedure was developed starting from commercially available

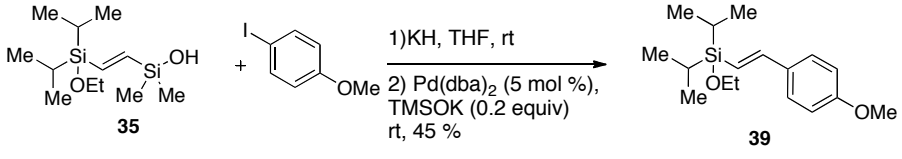
chlorodiisopropylsilane (Scheme 34). Ethynylmagnesium bromide addition into the chlorosilane afforded ethynyldiisopropylsilane, (**36**) in 70% yield. Chlorination followed by trapping with ethanol resulted in the desired ethoxysilane derivative **37** (90 %). Platinum-catalyzed hydrosilylation selectively added chlorodimethylsilane across the olefin and subsequent quenching with ethanol afforded the (*E*)-1,2-bissilyl ethene derivative **38**. Chemoselective hydrolysis of the less hindered silane with buffered acetic acid revealed the desired silanol in 95% yield.

Scheme 34



Attempts to form and isolate the potassium silanolate proved to be difficult as the salt readily dimerized upon concentration. However, keeping the preformed potassium silanolate in solution allowed for the stoichiometric preparation of this salt which could be used in the cross-coupling with 4-iodoanisole. Despite the discouragingly low yield (42%) obtained from this reaction, the desired compound was isolated as a stable compound. The low yield was attributed to the lack of reactivity and also instability of the starting material toward the reaction conditions (*vide infra*).

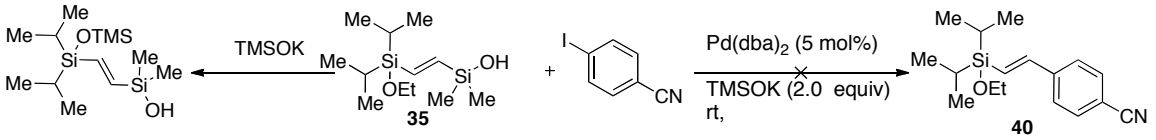
Scheme 35



4.3.2. Reactions with Aryl Iodides

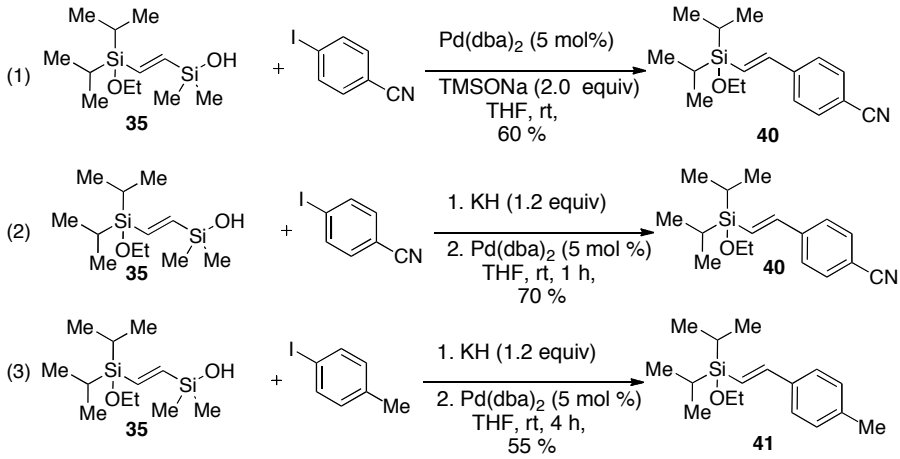
The cross-coupling reactions were first conducted with aryl iodides because of their ease of oxidative addition. The first studies were aimed to establish if forming the silanolate salt stoichiometrically was a necessary requirement in this cross-coupling reaction. Surprisingly, no desired product was detected employing TMSOK as the only basic additive in the reaction conditions. However, it was observed (GC/MS) that the TMSOK reacted with the silanol by displacing the ethoxy group on the diisopropylsilane moiety (Scheme 36).

Scheme 36



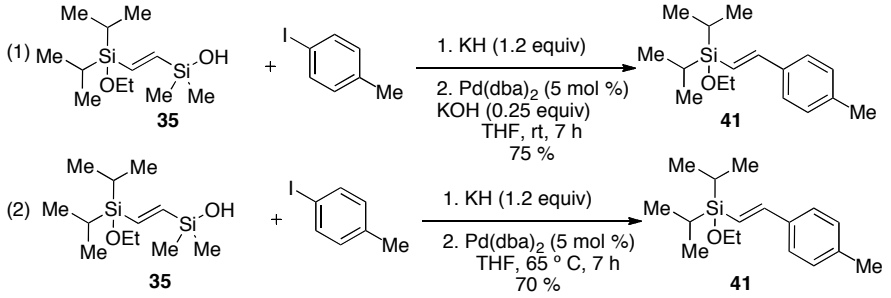
Gratifyingly, by using sodium trimethylsilanolate (TMSONa), much less disiloxane was observed and significant amounts of cross-coupling with the iodide was achieved (Scheme 37, eq1). When the reaction was carried out by preforming the silanolate stoichiometrically in the absence of a basic additive, significant amount of desired product was observed, albeit with incomplete consumption of the iodide (Scheme 37, eq. 2 and 3). Clearly, forming the silanolate stoichiometrically has a beneficial influence on the cross-coupling reaction; however, conditions were needed to facilitate complete consumption of the aryl iodide.

Scheme 37



Highly nucleophilic additives were not considered due to the displacement observed on the silicon center when using TMSOK; however, when the reactions were conducted in the presence of sub-stoichiometric amounts of potassium hydroxide significantly higher yields of the desired product were obtained (Scheme 38, eq 1). Carrying out the reactions in refluxing THF also led to higher yields of the desired products (Scheme 38, eq 2) .

Scheme 38

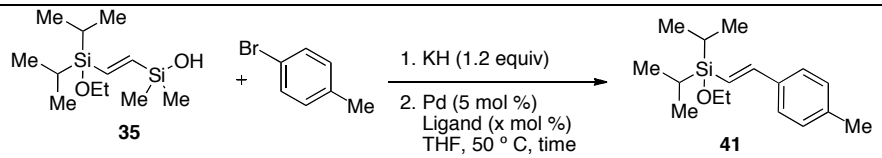


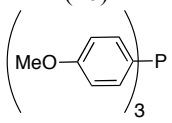
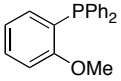
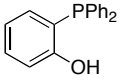
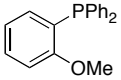
Despite the utility of cross-coupling with aryl iodides, it would be beneficial to utilize aryl bromides as substrates due to their lower costs and relative stability. Using the information from the initial cross-coupling with aryl iodides, further optimization was conducted on the coupling with aryl bromides.

4.3.3. Reactions with Aryl Bromides

Because of the greater strength of the carbon-bromine bond (80 kcal/mol)[60] compared to carbon-iodine bond (65 kcal/mol)[60] oxidative addition at palladium generally requires increased temperatures and/or electron rich ligands; therefore, a catalyst survey using a variety of phosphine and palladium precursors was undertaken (Table 14). Moderate conversion was observed employing APC and both triphenylphosphine and bidentate phosphine ligands (Table 14**,** entries 1 and 10-13). Electron rich phosphine ligands did not provide high yields of the desired products (Table 14, entries 2-6) and other palladium sources appeared to decrease the conversion compared to APC (Table 14, entries 14-20). Similar to the results of the previous studies, reduction of the bromide starting material as well as product isomerization were observed under the reaction conditions.

Table 14. Survey of Ligands and Palladium Precursors.

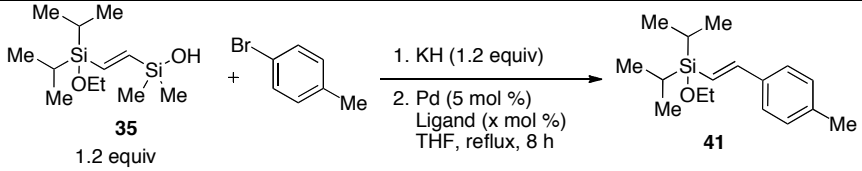


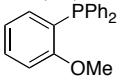
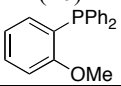
entry	Pd source	ligand, (mol %)	time, (h)	conversion,[a] (%)
1	APC	(10) Ph_3P	7	40
2	APC	(10) 	8	5
3	APC	(10) $(2\text{-tolyl})_3P$	8	1
4	APC	(10) Cy_3P	8	0
5	APC	(5) JohnPhos	8	0
6	APC	(5) S-Phos	8	10
7[b]	APC	(10) 	8	40
8	APC	(10) 	8	15
9	APC	(10) $(C_6F_5)_3P$	8	5
10	APC	(10) dppe	8	10
11	APC	(10) dppp	8	50
12	APC	(10) dpppentane	8	30
13	APC	(5) dppf	8	23
14	$Pd(dba)_2$	-	8	0
15	$Pd(dba)_2$	(10) Ph_3P	11	15
16	$Pd(dba)_2$	(5) dppp	8	0
17	$Pd(dba)_2$	(10) 	8	0
18	$Pd(dba\text{-}4,4'\text{-}OMe)_2$	-	8	0
19	$Pd(dba\text{-}4,4'\text{-}OMe)_2$	(10) Ph_3P	8	10
20[b]	$Pd(dba\text{-}4,4'\text{-}OMe)_2$	(5) dppp	8	15

a) Based on GC data using naphthalene as internal standard b) Product obtained as mixture of *E:Z* isomers.

Recalling the beneficial effect of additives and heat in the cross-coupling of aryl iodides, different temperatures and basic additives were investigated. Employing APC and $Pd(dba)_2$ with monodentate and bidentate phosphine ligands at reflux temperatures had little effect on the consumption of bromide (Table 15).

Table 15. Increased Temperature of Cross-Coupling.

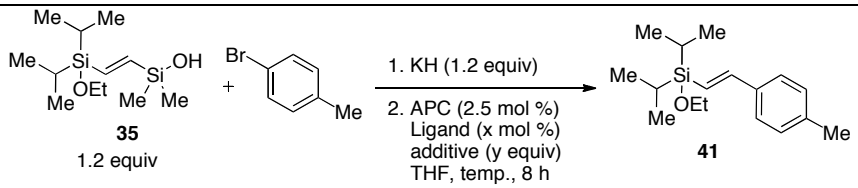


entry	Pd source	ligand, (mol %)	conversion,[a] (%)
1	APC	(10) Ph_3P	20
2	APC	(5) dppp	18
3	APC	(10) 	11
4	$Pd(dba)_2$	(10) Ph_3P	5
5	$Pd(dba)_2$	(5) dppp	2
6	$Pd(dba)_2$	(10) 	5

a) Based on GC data using naphthalene as internal standard

Using potassium hydroxide in the cross-coupling reaction at room temperature afforded none of the desired product (Table 16, entries 1-3). Gratifyingly, the use of KOH with APC and 1,3-bis(diphenylphosphino)propane (dppp) at 50 º led to completed conversion after 18 h (Table 16, entry 4)! Unfortunately, under these reaction conditions a small amount of product isomerization to the *cis* olefin was detected. Further optimization needed to be performed to discover conditions that afforded high yields of the desired product without significant isomerization of the olefin.

Table 16. Survey of Bases.

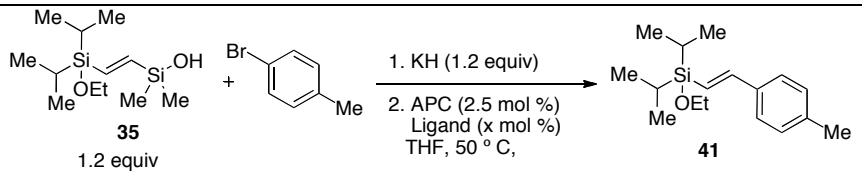


entry	ligand, (mol %)	additive (equiv)	temp, (° C)	conversion,[a] (%)
1	(5) dppp	(0.2) KOH	23	0
2	(10) Ph_3P	(0.2) KOH	23	0
3	(5) S-Phos	(0.2) KOH	23	0
4[b]	(5) dppp	(0.2) KOH	50	98
6	(5) dppp	(0.2) K_2CO_3	50	55
7	(5) S-Phos	(0.2) KOH	50	65

a) Based on GC data using naphthalene as internal standard b) Reaction was stirred for 18 h.

Incorporating a ligand that can easily dissociate from the palladium center allows a free coordination site to become available during transmetalation and removes steric interactions about the palladium caused by the ligand. Hemi-labile bisphosphine monoxide ligands were synthesized and surveyed to test this hypothesis. Bis(diphenylphosphino)butane monoxide (dppbO) worked very well and provided excellent conversion to the desired product (Table 17, entry 2)! The use of hemi-labile ligands would circumvent the need for additives so a variety of bisphosphine monoxide ligands were synthesized and tested in the cross-coupling reactions. Interestingly, using other bisphosphine monoxide ligands with different tether links resulted in lower yields of the desired products.

Table 17. Survey of Hemilabile Ligands.



entry	ligand, (mol %)	time, (h)	conversion,[a] (%)
1	(5) dppmO	9	25
2	(5) dppeO	4	61
3	(5) dpppO	6	55
4	(5) dppbO	6	85
5	(10) Ph_3PO	24	0
6	(5) dppfO	9	5
7	(5) BINAPO	9	5
8	(5) $dppeO_2$	6	50

a) Based on GC data using naphthalene as internal standard

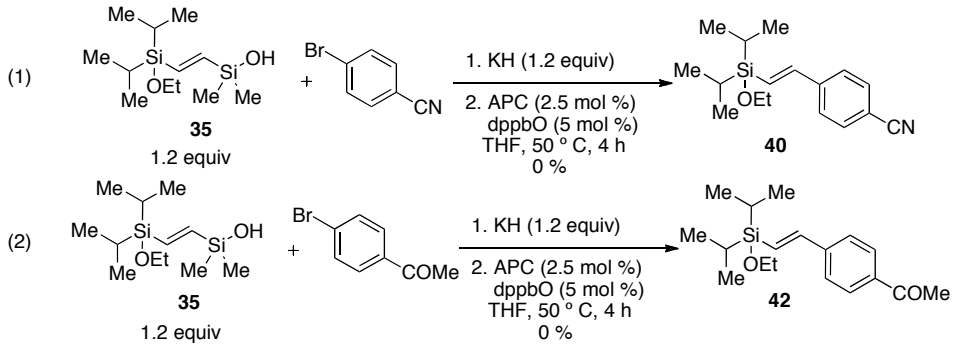
Having optimized the desired coupling with 4-bromotoluene the substrate scope with respect to bromide needed to be investigated. The objective to this project was to provide a facile route to polyenes and stilbene derivatives; therefore, numerous aryl bromides and alkenyl bromides were to be tested. It was observed that the reaction conditions developed above are not general and significant dimerization of the silanolate occurs when other aryl bromides are employed (*vide infra*).

4.3.4. Dimerization

Treatment of other aryl bromides under these reaction conditions yielded no desired product (Scheme 39). Also, the coupling with 4-bromotoluene was not reproducible, and for no reason. Numerous preparations of the silanol were undertaken incorporating normal phase and reverse phase chromatography to remove any trace impurities with no affect on the cross-coupling. Experiments were also performed in

which the catalyst and bromide were stirred for 30 minutes prior to addition of silanolate; however, these reactions also failed to provide the desired product.

Scheme 39



To gain insight into these failures NMR experiments were undertaken to study the stability of silanolate **35** in solution. The silanolate that was generated from the deprotonation with KH was unstable at elevated temperatures. Over the course of the reaction, the silanolate would decompose to unidentified polysiloxane products that are not competent in the cross-coupling reaction. The instability of the silanolate presents a major roadblock toward achieving the objective of this project. Further optimization, such as utilizing electron rich hemi-labile ligands, needs to be performed in order to obtain the desired products under mild conditions.

4.4. Discussion

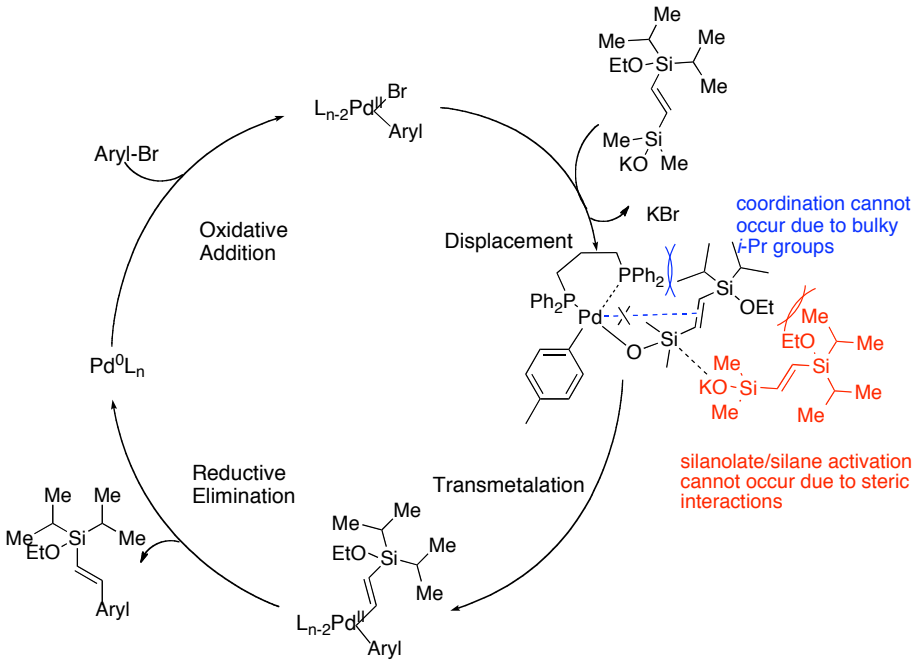
The preparation of a stable 1,2-bissilylethene unit was achieved and it was demonstrated to be a competent cross-coupling partner with aryl iodides at room temperature. Intriguingly, the silanol reacted with TMSOK to form a mixed disiloxane species (Scheme 36). This is surprising because the hypothesis was that the diisopropyl groups would prevent facile nucleophilic attack at this position. Gratifyingly, conditions

were developed using mild basic activation to facilitate conversion of the aryl iodide albeit with slight degree of isomerization of the product (Scheme 37).

When applying the cross-coupling conditions to aryl bromides, low yields of the desired product were obtained. Numerous phosphine ligands were surveyed to no avail (Table 14). Increasing the temperature and adding potassium hydroxide facilitated the conversion to the product (Table 16). It is proposed that the increased temperature is required for oxidative addition into a carbon-bromine bond and the activator needed is to facilitate transmetalation. The transmetalation is slow likely because of steric interactions in the transition complex arising from the bulk isopropyl groups of the distal silane.

Previous mechanistic studies reported that a coordination of the π-system in alkenylsilanols to the palladium center occurs prior to transmetalation,[61] which has also been reported during alkenyl-tin couplings.[37b] Because of the bulky diisopropyl ethoxy silane moiety, this interaction cannot occur and an external activation by a non-sterically encumbering nucleophile is required to induce an anionic activation to circumvent this steric interaction (Scheme 40). The role of the basic activator seems to implicate that the silanolate generated *in situ* cannot undergo activation by a second molecule of silanolate.

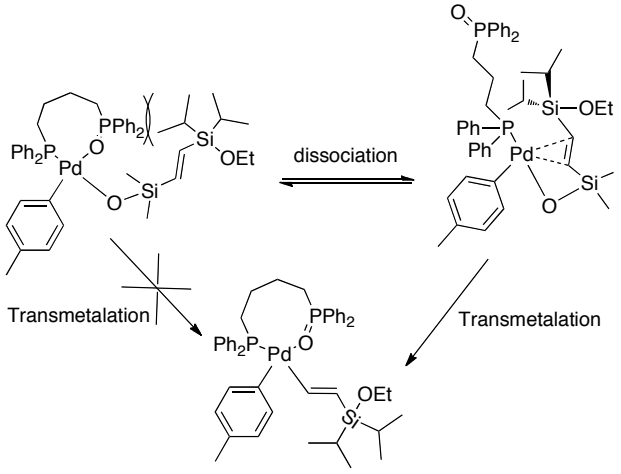
Scheme 40



The use of potassium hydroxide appeared to have a beneficial effect on the conversion observed in the cross-coupling reaction of **35** with aryl bromides. Unfortunately, under these conditions product isomerization occurred. The use of hemilabile ligands at elevated temperatures provided a route that allowed high conversions with lower amounts of isomerization. Hemilabile ligands facilitate transmetalation due to ease of dissociation from palladium following the displacement step. This dissociation allows a coordination site for the olefin to bind as well as removes the steric interactions associated with one of the ligands on palladium and the isopropyl groups on silicon (Scheme 41). The peculiar observation that dppbO gave rise to significantly higher conversions than the shorter tether equivalents can be explained by the binding affinity of the hemi-labile ligands (Table 17). Tether length influences inter- versus intramolecular binding at the metal center when bisphosphinopalladium monoxide ligands are employed.[62] When dppmO and dppeO are utilized stable 5- and 6-membered

P-Pd-O chelates can be formed in solution.[62-63] However, when using a longer tether, the intramolecular binding is significantly weaker because of the instability of forming larger ringed chelates. This instability contributes to the success of using dppbO in the cross-coupling reaction described above.

Scheme 41



The requirement of elevated temperatures is most likely due to the slower rate of oxidative addition into aryl bromides. Electron rich ligands facilitate this process and cross-coupling can be achieved at lower temperatures; however, none of the ligands tested resulted in high conversion under mild conditions. Elevated temperatures were shown to dimerize the silanolate over time to form a disiloxane species capable of chelating palladium and effectively poisoning the catalyst (Figure 4).[64] For this reaction to achieve high yields of the desired products, mild methods are needed to prevent this dimerization from occurring.

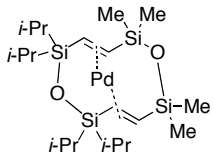


Figure 4. Disiloxane chelating palladium.

4.5. Conclusions and Outlook

The data collected from this work has led to the proposal of a mechanism for the cross-coupling of a 1,2-differentiated bissilylethene. However, the dimerization of the silanolate that occurs at prolonged elevated temperatures is a detrimental consequence of this approach. Further ligand screening or synthesis of other types of hemilabile ligands may alleviate the need for elevated temperatures. Electron rich hemilabile ligands should be tested in order to facilitate the oxidative addition of aryl bromides as well as transmetalation of the hindered silanolate.

Unfortunately, the modification of the silane structure seems constrained at this point because the limited reactivity associated with the large isopropyl groups about the distal silane. Increasing the steric interactions further would presumably inhibit the rate of transmetalation (*vide supra*). One possibility is to use trialkylsilanes in lieu of the diisopropylethoxysilane because of the increased stability when compared to alkoxy silanes (TMSOK exchange with ethoxy group). Trimethylsilane is a suitable derivative because of its ability to undergo fluoride promoted coupling as well as survive a plethora of reaction conditions (fluoride-free coupling). Additionally, the trimethylsilyl group would provide a less bulky environment for the transmetalation step during the fluoride-free coupling and may increase the rate of transmetalation.

Chapter 5. Experimental

5.1. General Experimental

All reactions were performed in oven-dried (140 °C) or flame dried glassware under an atmosphere of dry nitrogen or argon, unless noted. Reaction solvents tetrahydrofuran (Fisher, HPLC grade), diethyl ether (Fisher, BHT stabilized ACS grade) and methylene chloride (Fisher, unstabilized HPLC grade) were dried by percolation through two columns packed with neutral alumina under a positive pressure of argon. Reaction solvents hexane (Fisher, OPTIMA grade) and toluene (Fisher, ACS grade) were dried by percolation through a column packed with neutral alumina and a column packed with Q5 reactant, a supported copper catalyst for scavenging oxygen, under a positive pressure of argon. Reaction solvent acetonitrile (Fisher, HPLC grade) was used without further purification. DME and dioxane were distilled from Na and benzophenone. DMF was dried over activated 3 Å molecular sieves. Solvents for filtration and chromatography were certified ACS grade. Commercial reagents were purified by distillation or recrystallization prior to use. "Brine" refers to a saturated solution of sodium chloride. All reaction temperatures correspond to internal temperatures measured with Teflon coated thermocouples. Potassium hydride was washed with hexane and stored in a drybox. Sodium Hydride was washed with hexane and toluene and stored in a drybox.

^{1}H NMR spectra and ^{13}C NMR spectra were recorded on either a Varian Unity 400 (400 MHz, ^{1}H; 100 MHz, ^{13}C) or a Varian Unity 500 (500 MHz, ^{1}H; 125 MHz, ^{13}C) spectrometer. Spectra were referenced to residual chloroform (7.26 ppm, ^{1}H; 77.0 ppm,

^{13}C). Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). The prefix nfo (non-first order) coupling when used, indicates coupling which is not first order. Coupling constants, *J*, are reported in Hertz. Analytical thin-layer chromatography was performed on Merck silica gel plates with QF-254 indicator. Visualization was accomplished with UV (254), potassium permanganate (KMnO4) or iodine (I2). Column chromatography was performed using 230-400 mesh silica gel purchased from Silicycle or Aldrich.

Electron impact mass spectroscopy (EI) was performed at 70 eV. Data are reported in the form of m/z (intensity relative to base peak = 100). Infrared spectra (IR) peaks are reported in cm^{-1} with the indicated relative intensities: s (strong, 67-100%); m (medium, 34-66%); w (weak, 0-33%). Analytical capillary gas chromatography (GC) was performed using a gas chromatograph fitted with a flame ionization detector (H_2 carrier gas, 1 mL/min). Retention times (t_R) and integrated ratios were obtained using Agilent Chemstation Software. Sample injections were made using a PH 6890 Series Autosample Injector. Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus in sealed tubes and are corrected. Bulb-to-bulb distillations were performed on a Kugelrohr; boiling points (bp) corresponding to uncorrected air-bath temperatures (ABT).

Potassium trimethylsilanolate (Aldrich), potassium hydroxide (Aldrich), 2-(di-*t*-butylphosphino)biphenyl (Strem/Aldrich), tricyclohexylphosphine (Strem), 1,4-bis(diphenylphosphino)butane (Strem), palladium acetate (Strem), palladium chloride

(Pressure Chemical) triphenylphosphine oxide (Aldrich), triphenylarsine (Aldrich), alkynyl magnesium bromide (Aldrich), ethyl magnesium bromide (Aldrich), methyl lithium (Aldrich), were used as received. 4-Iodoanisole (Aldrich), 4-bromoanisole (Aldrich), 1-bromo-4-chlorobenzene (Aldrich), 1-bromonaphthalene (Aldrich), 4-bromobenzophenone (Aldrich), 4-bromo-3-methylanisole (Aldrich), 1-chloro-3-methyl-2-butene (Alfa Aesar), pivaldehyde (Aldrich), trichlorosilane (Gelest) were purchased from the respective vendor and purified either by distillation or recrystallization prior to use. A 1.0 M solution of tetra-*n*-butylammonium fluoride (TBAF) was made from the trihydrate salt purchased from Fluka or Acros, dissolved in dry THF, and stored under argon.

5.2. Literature Procedures

The following compounds were prepared according to literature procedure: allylpalladium chloride dimer,[65] bis(dibenzylideneacetone)palladium,[66] 1,2-bis(diphenylphosphino)methane monoxide,[67] 1,2-bis(diphenylphosphino)ethane monoxide,[67] 1,3-bis(diphenylphosphino)propane moxoxide,[67] 1,4-bis(diphenylphosphino)butane monoxide,[67] 1,1'-bis(diphenylphosphanyl) ferrocene monoxide[67] and 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl monoxide,[67] (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one and (1*E*,4*E*)-1,5-bis(4-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one,[68] (*E*)-ethyl 4-methylpent-2-enoate,[34] (*E*)-4-methylpent-2-en-1-ol,[35] (*E*)-1-chloro-4-methylpent-2-ene[36]

5.3. Chapter 3 Procedures

Response Factors and GC Methods

GC Method 1: Injections were made onto a Hewlett-Packard HP1 30-m capillary column. The injector temperature was 250 ºC and detector temperature was 300 ºC with a H_2 carrier gas flow of 16 mL/min. The column over temperature was as follows 100 ºC for 1 min, 100 ºC to 250 ºC ramp at 20 ºC/min, 250 ºC for 3 min, total run time 13.5 min. Response factors (R_f) for quantitative GC analysis for GC Method 1 were obtained by the equation below:

Eq1: Response factor for A = (area A * mmol biphenyl)/ (mmol A * area biphenyl)

1-(4-methylpent-1-en-3-yl)naphthalene **(8)**

mmol Biphenyl	Area Biphenyl	mmol **8**	Area **8**	Response Factor
0.0881	185207	0.0623	173098	1.32
0.0881	186816	0.0623	177097	1.34
0.0881	183554	0.0623	175448	1.35
0.101	317171	0.0685	290988	1.35
0.101	310126	0.0685	284303	1.35
0.101	320964	0.0685	295192	1.35
0.109	327955	0.0547	239686	1.45
0.109	314593	0.0547	230048	1.45

0.109	322677	0.0547	233443	1.44
			Avg	1.38

GC Method 2: Injections were made onto a Hewlett-Packard HP1 30-m capillary column. The injector temperature was 250 ºC and detector temperature was 300 ºC with a H_2 carrier gas flow of 16 mL/min. The column over temperature was as follows 100 ºC for 1 min, 100 ºC to 250 ºC ramp at 15 ºC/min, 250 ºC for 7 min, total run time 18 min.

GC Method 3: Injections were made onto a Hewlett-Packard HP1 30-m capillary column. The injector temperature was 250 ºC and detector temperature was 300 ºC with a H_2 carrier gas flow of 16 mL/min. The column over temperature was as follows 100 ºC for 2 min, 100 ºC to 240 ºC ramp at 18 ºC/min, 240 ºC for 5 min, total run time 14.8 min. Response factors (R_f) for quantitative GC analysis for GC Method 1 were obtained by the equation below:

Eq1: Response factor for A = (area A * mmol biphenyl)/ (mmol A * area biphenyl)

mmol Biphenyl	Area Biphenyl	mmol 4-bromotoluene	Area 4-bromotoluene	Response Factor
0.0901	198236	0.198	221081	0.50
0.0901	202417	0.198	224153	0.50
0.0901	198996	0.198	216556	0.49
0.105	282804	0.120	194618	0.60
0.105	300765	0.120	199161	0.57

0.105	308456	0.120	201242	0.57
			Avg.	0.53

1-methyl-4-(2-methylbut-3-en-2-yl)benzene **(19)**

mmol Biphenyl	Area Biphenyl	mmol **19**	Area **19**	Response Factor
0.112	151416	0.0618	59935	0.71
0.112	151631	0.0618	59596	0.71
0.112	103241	0.0618	42841	0.75
0.0687	186114	0.0549	103053	0.69
0.0687	193963	0.0549	108666	0.70
0.0687	204805	0.0549	114114	0.69
			Avg.	0.71

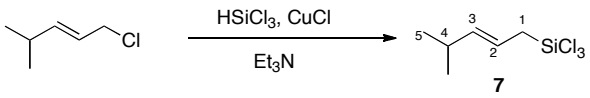
Heck-coupled product

mmol Biphenyl	Area Biphenyl	mmol **19-Heck**	Area **19-Heck**	Response Factor
0.124	184573	0.0463	110302	1.60
0.124	185822	0.0463	111453	1.60
0.124	186848	0.0463	111276	1.59
0.149	366120	0.0507	188870	1.51

0.149	371172	0.0507	192177	1.52
0.149	365767	0.0507	186461	1.50
0.0785	162481	0.0260	87515	1.62
0.0785	160616	0.0260	86344	1.62
0.0785	162804	0.0260	87258	1.61
			Avg.	1.58

Scheme 14

Preparation of (*E*)-Trichloro(4-methylpent-2-en-1-yl)silane, (7)



7

To a two-necked, 25-mL, round-bottomed flask equipped with septa was added a solution of (*E*)-1-chloro-4-methylpent-2-ene (4.178 g, 35 mmol) and trichlorosilane (5.3 mL, 52.8 mmol, 1.5 equiv) in diethyl ether (8 mL) via syringe cooled in an ice bath under argon. The solution was transferred via canula to a three-necked, 250 mL, round-bottomed flask equipped with a magnetic stir bar, and septa containing CuCl (208 mg, 2.1 mmol, 0.06 equiv) and triethylamine (5.9 mL, 42 mmol, 1.2 equiv) in diethyl ether (15 mL) cooled in an ice bath under argon. The internal temperature remained below 5 ºC during the addition and a white smoke appeared as the addition occurred. The flask was purged with N_2 for 15 min following the addition before allowing the reaction to warm to room temperature over 4 h. The reaction was filtered through a dried, washed Celite (15 g) and the pad was washed with diethyl ether (150 mL). The filtrate was concentrated at 1 atm to afford a yellow oil. Purification by fractional distillation to afford 5.3 g (70 %)

colorless oil.

Data for **7**:

bp: 65 ºC (17 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

5.55 (dd, *J* = 15.6 and 7.2, 1 H, HC(3)), 5.28 (m, 1 H, HC(2)), 2.29 (m, 1 H HC(4)), 2.23 (d, *J* = 8.0, 2 H, HC(1)), 0.98 (d, *J* = 7.2, 6 H, HC(5)).

Preparation of (*E*)-Chlorodimethyl(4-methylpent-2-en-1-yl)silane

To a three-necked, 250-mL, round-bottomed flask equipped with a magnetic stir bar, addition funnel (120-mL), and septa was added a solution of (*E*)-trichloro(4-methylpent-2-en-1-yl)silane (5.116 g, 23.51 mmol) in diethyl ether (63 mL) via syringe under argon. The solution was stirred as methyllithium (32 mL, 47 mmol, 2.0 equiv, 1.47 M solution in diethyl ether) and diethyl ether (31 mL) were added dropwise via the addition funnel over 1 h at rt. After an additional hour of stirring the reaction mixture was filtered through Celite (15 g) and the filtrate was concentrated *in vacuo* to afford a colorless oil. Purification by fractional distillation to afford 2.0 g (50 %) of colorless oil.

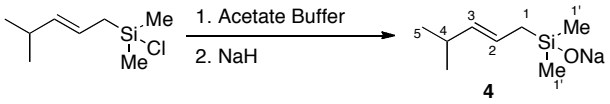
Data for (*E*)-Chlorodimethyl(4-methylpent-2-en-1-yl)silane:

bp: 62 ºC (17 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

5.34 (m, 2 H, HC(2), HC(3)), 2.26 (m, 1 H HC(4)), 1.71 (d, *J* = 6.0, 2 H, HC(1)), 0.97 (d, *J* = 6.5, 6 H, HC(5)), 0.40 (s, 6 H, HC(1')).

Preparation of Sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (4)



4

To a one-necked, 125-mL, round-bottomed flask equipped with a magnetic stir bar was added acetate buffer (27 mL, 1 M, pH 5) under argon. (*E*)-chlorodimethyl(4-methylpent-2-en-1-yl)silane (0.7286 g, 4.1 mmol) in diethyl ether (6 mL) was added via syringe and was stirred. After 15 min the mixture was transferred to a separatory funnel and extracted with diethyl ether (3 x 100 mL) and the combined organic extracts were washed with $NaHCO_3$ (100 mL), water (100 mL), and brine (100 mL). The combined organic phases was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to a volume of 5 mL. The crude solution was purified immediately by column chromatography (pentane/diethyl ether (4:1), SiO_2, 20 mm x 100 mm) to remove silane impurities. The pure material was transferred as a solution in hexane (5 mL) to a single-necked round-bottomed flask. The solution was then added dropwise over 5 minutes to a Schlenk flask containing a slurry of NaH (487 mg, 20.3 mmol, 1.2 equiv) in hexane (20 mL). Upon complete addition the reaction was allowed to stir for 30 minutes before being filtered through a fritted glass funnel (medium porosity). The filtrate was concentrated *in vacuo* to afford 517 mg (70 %) white solid.

Data for **4**:

^{1}H NMR: (500 MHz, d_6-benzene)

5.72 (m, 1 H, HC(2)), 5.44 (dd, J = 15.0 and 7.0, 1 H, HC(3)), 2.32 (h, J = 7, 1 H HC(4)), 1.56 (d, J = 8.0, 2 H, HC(1)), 1.05 (d, J = 6.5, 6 H, HC(5)), 0.16 (s, 6 H, HC(1')).

General Procedure I: Cross-coupling of 1-Bromonaphthalene with Sodium (*E*)-Dimethyl(4-methylpent-2-en-1-yl)silanolate:

Table 2, Entry 1

To an oven-dried, 5-mL, 1-piece, round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (74 mg, 0.2 mmol, 0.2 equiv) and palladium(II) trifluoroacetate (16.6 mg, 0.05 mmol, 0.05 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (361 mg, 2.0 mmol, 2 equiv), 1-bromonaphthalene (207 mg, 1.0 mmol) in toluene (4 mL) was added to the flask. The resulting mixture was heated to 70 ºC in an oil bath for 30 h. The reaction was then allowed to cool to room temperature. Diethyl ether (20 mL) was added and the mixture was filtered through a short pad of silica gel (5 g). The silica pad was washed with diethyl ether (100 mL) and the filtrates were concentrated *in vacuo* to afford 524 mg of crude material. Purification by column chromatography (pentane for 3 column volumes then pentane:diethyl ether (4:1), SiO_2, 290 mm x 20 mm) gave 147 mg (70 %, 1:66 α:γ) of **8** as a colorless oil.

Table 2 Entry 2

Following General Procedure I, allylpalladium chloride dimer (1.8 mg, 0.005 mmol, 0.025 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), biphenyl (17.3 mg, 0.112 mmol), 1-bromonaphthalene (41.4 mg, 0.2 mmol) and sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 12 h. An aliquot

of the reaction mixture was analyzed by GC method 1. **8** γ-t_R= 6.71 min (70 %), α-t_R=6.97 min (1:33 α:γ ratio)

Table 2, Entry 3

Following General Procedure I, allylpalladium chloride dimer (1.8 mg, 0.005 mmol, 0.025 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.2 mg, 0.04 mmol, 0.2 equiv), biphenyl (12.4 mg, 0.0804 mmol), 1-bromonaphthalene (41.4 mg, 0.2 mmol) and sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 12 h. An aliquot of the reaction mixture was analyzed by GC method 1. **8** γ-t_R= 6.71 min (82 %), α-t_R=6.97 min (1:38 α:γ ratio)

Table 2, Entry 4

Following General Procedure I, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), norbornadiene (1.0 μL, 0.01 mmol, 0.05 equiv), biphenyl (6.1 mg, 0.03956 mmol), 1-bromonaphthalene (41.4 mg, 0.2 mmol) and sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 12 h. An aliquot of the reaction mixture was analyzed by GC method 2. **8** γ-t_R= 8.43 min (80 %), α-t_R=8.94 min (1:32 α:γ ratio)

General Procedure II: Cross-coupling of Aryl Bromides with Sodium (*E*)-Dimethyl(4-methylpent-2-en-1-yl)silanolate:

Table 3 Entry 1

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added norbornadiene

(1.0 μL, 0.01 mmol, 0.05 equiv) and bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2 equiv), 4-bromobenzophenone (52.2 mg, 0.2 mmol) in toluene (0.4 mL) prepared in a glove box in a Schlenk flask was sealed and placed on a manifold where the headspace was evacuated and refilled with argon. The solution was then added to the reaction flask by canula. The resulting mixture was heated to 70 ºC in an oil bath for 12 h. An aliquot of the reaction mixture was filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 2. **9** γ-t_R= 11.97 min (100 %), α-t_R=12.31 min (1:2 α:γ ratio)

Table 3 Entry 2

Following General Procedure II, norbornadiene (1.0 μL, 0.01 mmol, 0.05 equiv) and bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv), and 4 bromobenzotrifluoride (45.0 mg, 0.2 mmol) in toluene (0.4 mL) was stirred at 70 ºC for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **10** γ-t_R= 4.01 min (100 %), α-t_R=4.54 min (1:1.24 α:γ ratio)

Table 3 Entry 3

Following General Procedure II, norbornadiene (1.0 μL, 0.01 mmol, 0.05 equiv) and bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv), and 4 bromoanisole (37.4 mg, 0.2 mmol) in toluene (0.4 mL) was stirred at 70 ºC for 8 h. An

aliquot of the reaction mixture was analyzed by GC method 2. **11** γ-t_R= 6.11 min (20 %), α-t_R=6.99 min (3.5:1 α:γ ratio)

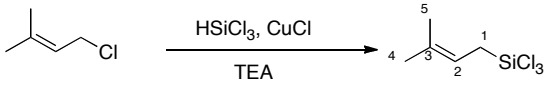
Table 3 Entry 4

Following General Procedure II, norbornadiene (1.0 μL, 0.01 mmol, 0.05 equiv) and bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv), and 2 bromotoluene (34.2 mg, 0.2 mmol) in toluene (0.4 mL) was stirred at 70 ºC for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **12** γ-t_R= 4.66 min (80 %), α-t_R=5.26 min (1:18 α:γ ratio)

Table 3 Entry 5

Following General Procedure II, norbornadiene (1.0 μL, 0.01 mmol, 0.05 equiv) and bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv), and 4-bromo-3-methylanisole (40.2 mg, 0.2 mmol) in toluene (0.4 mL) was stirred at 70 ºC for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **13** γ-t_R= 6.89 min (10 %), α-t_R=7.28 min (1:10 α:γ ratio)

Preparation of Trichloro(3-methylbut-2-en-1-yl)silane (14)



14

To a two-necked, 25-mL, round-bottomed flask equipped with septa was added via syringe a solution of (*E*)-1-chloro-3-methylbut-2-ene (2.360 g, 22.57 mmol) and trichlorosilane (3.2 mL, 31.59 mmol, 1.4 equiv) in diethyl ether (8 mL) cooled in an ice bath under argon. The solution was transferred via canula to a three-necked, 250-mL,

round-bottomed flask equipped with a magnetic stir bar, and septa containing CuCl (214 mg, 2.17 mmol, 0.096 equiv) and triethylamine (3.8 mL, 27.08 mmol, 1.2 equiv) in diethyl ether (8 mL) cooled in an ice bath under argon. The internal temperature remained below 5 ºC during the addition and a white smoke appeared as the addition occurred. The flask was purged with N_2 for 15 min following the addition before allowing the reaction to warm to room temperature over 4 h. The reaction was filtered through a dried, washed Celite (15 g) and the pad was washed with diethyl ether (150 mL). The filtrate was concentrated at 1 atm to afford a yellow oil. Purification by fractional distillation to afford 2.905 g (64 %) colorless oil.

Data for **14**:

bp: 82 ºC (100 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

5.14 (m, 1 H, HC(2)), 2.29 (d, J = 8.5, 2 H, HC(2)), 1.77 (s, 3 H, HC(4)), 1.66 (s, 3 H, HC(5)).

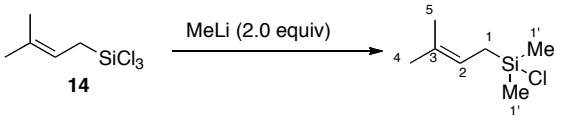
^{13}C NMR: (126 MHz, $CDCl_3$)

136.3 (C(3)), 112.2 (C(2)), 25.8 (C(4)), 25.6 (C(5)), 18.0 (C(1))

IR: (film)

3605 (w), 2975 (m), 2916 (m), 1618 (w), 1449 (w), 1378 (w), 1174 (s), 1153 (s), 820 (m), 756 (s), 722 (s)

Preparation of Chlorodimethyl(3-methylbut-2-en-1-yl)silane



To a three-necked, 500-mL, round-bottomed flask equipped with a magnetic stir bar, addition funnel, and septa was added trichloro(3-methylbut-2-en-1-yl)silane (18.204 g, 89.42 mmol) in diethyl ether (276 mL) under argon. The solution was stirred as methyl lithium (110 mL, 174 mmol, 1.95 equiv, 1.59 M solution in diethyl ether) and diethyl ether (120 mL) were added dropwise via addition funnel over 1 h. After an additional hour of stirring the reaction mixture was filtered through Celite (15 g) and filtrate concentrated *in vacuo* to afford a colorless oil. Purification by fractional distillation to afford 10.2 g (70 %) colorless oil.

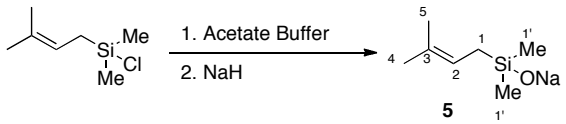
Data for Chlorodimethyl(3-methylbut-2-en-1-yl)silane:

bp: 73 ºC (100 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

5.13 (m, 1 H, HC(2)), 1.72 (m, 5 H, HC(1), HC(4)), 1.59 (s, 3 H, HC(5)), 0.39 (s, 6 H, HC(1'))

Preparation of Sodium Dimethyl(3-methylbut-2-en-1-yl)silanolate (5)



To a one-necked, 125-mL, round-bottomed flask equipped with a magnetic stir bar was added acetate buffer (96 mL, 1 M aqueous solution, pH 5) under argon. Chlorodimethyl(3-methylbut-2-en-1-yl)silane (2.425 g, 14.6 mmol) in diethyl ether (21

mL) was added via syringe and stirred. After 15 min the mixture was extracted with diethyl ether (3 x 100 mL) and combined organic extracts washed with $NaHCO_3$ (100 mL), water (100 mL), and Brine (100 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to a volume of 5 mL. The crude solution was purified immediately by column chromatography (pentane/diethyl ether (9:1), SiO_2, 20 mm x 100 mm) to remove silane impurities. The pure material was transferred as a solution in hexane (5 mL) to a single-necked round-bottomed flask. The solution was then added dropwise over 5 minutes to a Schlenk flask containing a slurry of NaH (420 mg, 17.5 mmol, 1.2 equiv) in hexane (15 mL). Upon complete addition the reaction was allowed to stir for 30 minutes before filtering through a fritted glass funnel (medium porosity). The filtrate was concentrated *in vacuo* to afford 1.8 g (75 %) white solid.

Data for **5**:

^{1}H NMR: (500 MHz, d_6-benzene)

5.47 (m, 1 H, HC(2)), 1.80 (s, 3 H, HC(4)), 1.69 (s, 3 H, HC(5)), 1.53 (d, J = 8.5, 2 H, HC(1)), 0.17 (s, 6 H, HC(1')).

General Procedure III: Cross-coupling of 1-Bromonaphthalene with Sodium Dimethyl(3-methylbut-2-en-1-yl)silanolate:

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added ligand and palladium precursor. The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv),

1-bromonaphthalene (41.4 mg, 0.2 mmol) in toluene (0.4 mL) prepared in a glove box in a Schlenk flask was sealed and placed on a manifold where the headspace was evacuated and refilled with argon. The solution was then added to the reaction flask by canula. The resulting mixture was heated to 70 ºC in an oil bath and reaction progress monitored by GC. An aliquot of the reaction mixture was filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 2.

Table 4 Entry 1

Following General Procedure III, norbornadiene (1.0 μL, 0.01 mmol, 0.05 equiv), bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv) 1-bromonaphthalene (41.4 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 30 h. An aliquot of the reaction mixture was analyzed by GC method 2. **15** γ-t_R= 7.96 min, α-t_R=8.74 min (98 % yield including both isomers, 1.3:1 α:γ ratio)

Table 4 Entry 2

Following General Procedure III, palladium(II) trifluoroacetate (3.3 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.2 mg, 0.04 mmol, 0.2 equiv), 1-bromonaphthalene (41.4 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 14 h. An aliquot of the reaction mixture was analyzed by GC method 2. **15** γ-t_R= 7.96 min, α-t_R=8.74 min (98 % yield including both isomers, 1:4.7 α:γ ratio)

Table 4 Entry 3

Following General Procedure III, palladium(II) trifluoroacetate (3.3 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), 1-bromonaphthalene (41.4 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 14 h. An aliquot of the reaction mixture was analyzed by GC method 2. **15** γ-t_R= 7.96 min, α-t_R=8.74 min (88 % yield including both isomers, 1:3 α:γ ratio)

Table 4 Entry 4

Following General Procedure III, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.2 mg, 0.04 mmol, 0.2 equiv), 1-bromonaphthalene (41.4 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 14 h. An aliquot of the reaction mixture was analyzed by GC method 2. **15** γ-t_R= 7.96 min, α-t_R=8.74 min (92 % yield including both isomers, 1:4.3 α:γ ratio)

Table 4 Entry 5

Following General Procedure III, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), 1-bromonaphthalene (41.4 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 14 h. An aliquot of the reaction mixture was analyzed by

GC method 2. **15** γ-t_R= 7.96 min, α-t_R=8.74 min (83 % yield including both isomers, 1:5.7 α:γ ratio).

General Procedure IV: Cross-coupling of Aryl bromides with Sodium Dimethyl(3-methylbut-2-en-1-yl)silanolate

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), and (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv), aryl bromide in toluene (0.4 mL) prepared in a glove box in a Schlenk flask was sealed and placed on a manifold where the headspace was evacuated and refilled with argon. The solution was then added to the reaction flask by canula. The resulting mixture was heated to 70 ºC in an oil bath and reaction progress monitored by GC. An aliquot of the reaction mixture was filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 2.

Table 5 Entry 1

Following General Procedure IV, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), 4-bromobenzophenone (52.2 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 14 h. An aliquot of the reaction mixture was

analyzed by GC method 2. **16** γ-t_R= 11.50 min, α-t_R=12.09 min (100 % yield including both isomers, 1:5.6 α:γ ratio)

Table 5 Entry 2

Following General Procedure IV, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), 4-bromobenzonitrile (36.4 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 48 h. An aliquot of the reaction mixture was analyzed by GC method 2. **17** γ-t_R= 6.02 min, α-t_R=6.21 min (42 % yield including both isomers, 1:6 α:γ ratio)

Table 5 Entry 3

Following General Procedure IV, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), 4-bromobenzotrifluoride (45.0 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC method 2. **18** γ-t_R= 3.31 min, α-t_R=4.11 min (80 % yield including both isomers, 1:8 α:γ ratio)

Table 5 Entry 4

Following General Procedure IV, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), 4-bromoanisole (37.4 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4

mL) were stirred at 70 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC method 2. **19** γ-t_R= 5.42 min, α-t_R=6.01 min (60 % yield including both isomers, 1:6 α:γ ratio)

Table 5 Entry 5

Following General Procedure IV, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), 4-bromo-3-methylanisole (40.2 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 28 h. An aliquot of the reaction mixture was analyzed by GC method 2. **20** γ-t_R= 6.54 min, α-t_R=7.01 min (50 % yield including both isomers, 1:10 α:γ ratio)

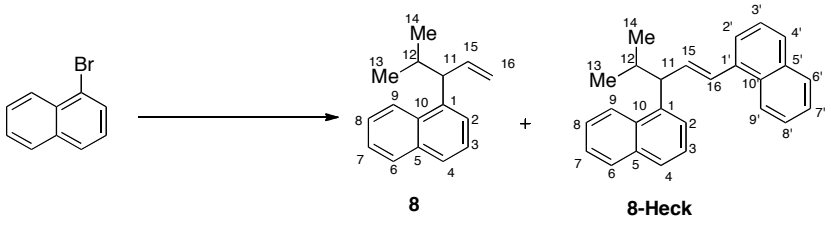
Table 5 Entry 6

Following General Procedure IV, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), 4-bromobenzonitrile (36.4 mg, 0.2 mmol) and sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2 equiv) in toluene (0.4 mL) were stirred at 90 ºC for 13 h. An aliquot of the reaction mixture was analyzed by GC method 2. **21** γ-t_R= 6.02 min, α-t_R=6.21 min (42 % yield including both isomers, 1:6 α:γ ratio)

General Procedure V: Preparative Cross-coupling of Sodium (*E*)-Dimethyl(4-methylpent-2-en-1-yl)silanolate and Aryl Bromides

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added bis(dibenzylideneacetone)palladium (28.8 mg, 0.05 mmol, 0.05 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (361 mg, 2.0 mmol, 2 equiv), aryl bromide (207 mg, 1.0 mmol), and norbornadiene (4.6 mg, 0.05 mmol, 0.05 equiv) in toluene (4 mL) was added to the flask. The resulting mixture was heated to 70 ºC in an oil bath. After complete consumption of the bromide the reaction was then allowed to cool to room temperature. Diethyl ether (20 mL) was added and the mixture was filtered through a short pad of silica gel (5 g). The silica pad was washed with diethyl ether (100 mL) and the filtrates were concentrated *in vacuo* to afford the crude material. Purification by column chromatography followed by Kugelrohr distillation to afford the desired product.

Scheme 16. Preparation of 1-(4-Methylpent-1-en-3-yl)naphthalene (8) and (8-Heck)



Following General Procedure V, bis(dibenzylideneacetone)palladium (28.8 mg, 0.05 mmol, 0.05 equiv.), *E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (361 mg, 2.0 mmol, 2 equiv), 1-bromonaphthalene (207 mg, 1 mmol), and norbornadiene (4.6 mg, 0.05 mmol, 0.05 equiv) in 4 mL of toluene was stirred under argon at 70 ºC in an oil bath.

After 18 h GC analysis indicated that no bromide remained and the reaction was allowed to cool to room temperature. Diethyl ether (15 mL) was added and the mixture was filtered through a pad of silica gel (5 g). The pad was rinsed with diethyl ether (100 mL) and the combined filtrates were concentrated *in vacuo* to afford 270 mg of crude material. Purified by column chromatography (hexane for 4 column volumes then hexane/ethyl acetate (10:1), SiO_2, 20 mm x 290 mm) and Kugelrohr distillation to afford 107 mg (50 %) colorless oil.

Data for **8**:

bp: 150 ºC (0.5 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

8.16 (d, J =8.3, 1 H HC(9)), 7.86 (d, J = 8.1, 1 H, HC(6)), 7.72 (d, J =7.8, 1 H, HC(4)), 7.51-7.43 (m, 3 H, HC(2), HC(3), HC(7), HC(8)), 6.17-6.11 (m, 1 H, HC(15)), 5.12-5.05 (m, 2 H, HC(16)), 3.80 (at, J = 8.7, 1 H HC(11)), 2.19 (hept, J = 6.8, 1 H, HC(12)), 1.06 (d, J = 7.6, 3 H, HC(13) or HC(14)), 0.82 (d, J = 6.6, 3 H, HC(13) or HC(14)).

^{13}C NMR: (126 MHz, $CDCl_3$)

140.9 (C(15)), 140.7 (C(1)), 134.3 (C(5)), 132.1 (C(10)), 129.2 (C(6)), 126.7 (C(4)), 125.9 (C(3)), 125.7 (C(9)), 125.5 (C(7)), 124.6 (C(8)), 123.7 (C(2)), 115.7 (C(16)), 52.6 (C(11)), 32.9 (C(12)), 21.6 (C(13) or (C(14)), 20.88 (C(13) or (C(14)).

IR: (film)

3072 (m), 2960 (m), 2865 (s), 1637 (m), 1610 (m), 1512 (s), 1464 (m), 1394 (m), 1369 (m), 1170 (m), 992 (m), 913 (s)

GC: γ-t_R: 8.45 min (GC Method 2)

TLC: R_f= 0.26 (hexane) [silica gel, UV]

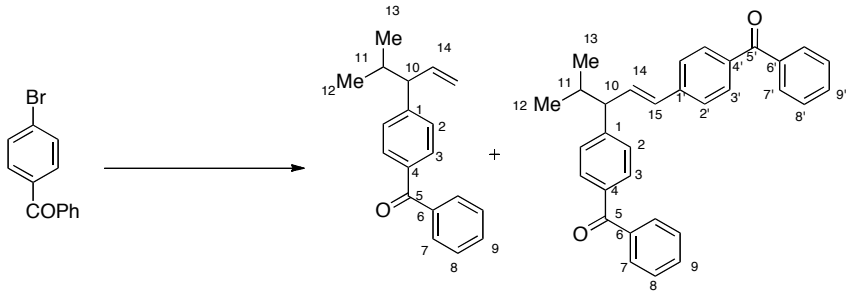
Data for **8-Heck**:

^{1}H NMR: (500 MHz, $CDCl_3$)

8.31 (d, *J* = 8.5, 1 H, HC(9) or HC(9')), 8.04 (m, 1 H, HC(aryl)), HC(d, *J* = 8, 1 H, HC(6) or HC(6')), 7.82 (m, 1 H, HC(aryl)), 7.74 (m, 2 H, HC(aryl)), 7.50 (m, 8 H, HC(aryl)), 7.24 (d, *J* = 15, 1 H, HC(16)), 6.57 (dd, *J* = 15 and 9, 1 H, HC(15)), 4.16 (at, *J* = 8.5, 1 H, HC(11)), 2.34 (m, 1 H, HC(12)), 1.17 (d, *J* = 6.5, 3 H, HC(13) or HC(14)), 0.94 (d, *J* = 7, 3 H, HC(13) or HC(14)).

TLC: R_f= 0.22 (hexane) [silica gel, UV]

Scheme 17. Preparation of (4-(4-Methylpent-1-en-3-yl)phenyl)(phenyl)methanone (9) and (9-Heck)



Following General Procedure V, bis(dibenzylideneacetone)palladium (28.8 mg, 0.05 mmol, 0.05 equiv.), (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (361 mg, 2.0 mmol, 2 equiv), 4-bromobenzophenone (261 mg, 1 mmol), and norbornadiene (4.6 mg, 0.05 mmol, 0.05 equiv) in 4 mL of toluene was stirred under argon at 70 ºC in an oil bath. After 18 h GC analysis indicated that no bromide remained and the reaction was

allowed to cool to room temperature. Diethyl ether (15 mL) was added and the mixture was filtered through a pad of silica gel (5 g). The pad was rinsed with diethyl ether (100 mL) and the combined filtrates were concentrated *in vacuo* to afford 480 mg of crude material. Purified by column chromatography (hexane for 4 column volumes then hexane/ethyl acetate (10:1), SiO_2, 20 mm x 290 mm) and Kugelrohr distillation to afford 192 mg (73 %) colorless oil.

Data for **9**:

bp: 237 ºC (0.5 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

7.79 (m, 4 H, HC(3), HC(7)), 7.58 (m, 1 H, HC(9)), 7.47 (m, 2 H, HC(8)), 7.29 (m, 2 H, HC(2)), 6.01 (m, 1 H, HC(14)), 5.07 (m, 2 H, HC(16)), 2.99 (t, J = 9.0, 1 H, HC(10)), 2.32 (m, 1 H, HC(11)), 0.98 (d, J = 7.0, 3 H, HC(12) or HC(13)), 0.78 (d, J = 7.0, 3 H HC(12) or HC(13)).

^{13}C NMR: (126 MHz, $CDCl_3$)

196.7 (C(5)), 149.8 (C(6)), 140.5 (C(7)), 138.1 (C(4), 135.6 (C(1)), 132.4 (C(14)), 130.7 (C(9)), 130.2 (C(8)), 128.5 (C(3)), 128.0 (C(2)), 124.9 (C(15)), 39.2 (C(10)), 31.2 (C(11)), 21.3 (C(12) or (C(13)), 20.9 (C(12) or (C(13)).

Analysis: $C_{19}H_{20}O$ (264.36)

Calcd: C, 86.32, H, 7.63

Found: C, 85.93 H, 7.69

GC: γ-t_R: 11.99 min (GC Method 2)

TLC: R_f= 0.39 (hexane/ethyl acetate 10:1) [silica gel, UV]

Data for **9-Heck**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.78 (m, 9 H, HC(aryl)), 7.58 (m, 2 H, HC(aryl)), 7.47 (m, 7 H, HC(aryl)), 7.36 (d, *J* = 8, 1 H, HC(15)), 6.53 (m, 1 H, HC(14)), 3.18 (at, *J* = 9, 1 H, HC(10), 2.22 (m, 1 H, HC(11)), 1.06 (d, *J* = 3.5, 3 H, HC(12) or HC(13)), 0.78 (d, *J* = 6.5, 3 H HC(12) or HC(13)).

TLC: R_f= 0.28 (hexane/ethyl acetate 10:1) [silica gel, UV]

General Procedure VI: Cross-coupling of Sodium (*E*)-Dimethyl(4-methylpent-2-en-1-yl)silanolate and 4-Bromobenzophenone with TMSOK

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv), 4-bromobenzophenone (52.2 mg, 0.2 mmol), and norbornadiene (1 μL, 0.01 mmol, 0.05 equiv) in toluene (2 mL) was added to the flask and stirred. A solution of potassium trimethyl silanolate (TMSOK) in toluene (2 mL) was then added by syring. The resulting mixture was heated to 70 ºC in an oil bath. An aliquot of the reaction mixture was filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 2.

Scheme 6 Entry 1

Following General Procedure VI, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv), 4-bromobenzophenone (52.2 mg, 0.2 mmol), norbornadiene (1 μL, 0.01 mmol, 0.05 equiv), TMSOK (6.4 mg, 0.05 mmol, 0.25 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 7 h. An aliquot of the reaction mixture was analyzed by GC method 2. **9** γ-t_R= 11.96 min, α-t_R=12.31 min (100 % yield including both isomers, 1.3:1 α:γ ratio)

Scheme 6 Entry 2

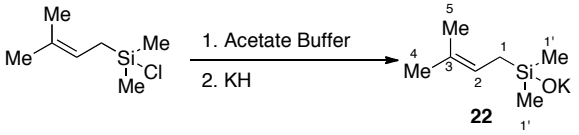
Following General Procedure VI, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv), 4-bromobenzophenone (52.2 mg, 0.2 mmol), norbornadiene (1 μL, 0.01 mmol, 0.05 equiv), TMSOK (12.8 mg, 0.10 mmol, 0.50 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 16 h. An aliquot of the reaction mixture was analyzed by GC method 2. **9** γ-t_R= 11.96 min, α-t_R=12.31 min (100 % yield including both isomers, 1.6:1 α:γ ratio)

Scheme 6 Entry 3

Following General Procedure VI, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), sodium (*E*)-dimethyl(4-methylpent-2-en-1-yl)silanolate (72.1 mg, 0.4 mmol, 2.0 equiv), 4-bromobenzophenone (52.2 mg, 0.2 mmol), norbornadiene (1 μL, 0.01 mmol, 0.05 equiv), TMSOK (25.7 mg, 0.2 mmol, 1.0 equiv) in toluene (0.4 mL) were stirred at 70 ºC for 50 h. An aliquot of the reaction mixture was analyzed by GC

method 2. **9** γ-t_R= 11.96 min, α-t_R=12.31 min (100 % yield including both isomers, 1.8:1 α:γ ratio)

Preparation of Potassium Dimethyl(3-methylbut-2-en-1-yl)silanolate (22)



22

To a one-necked, 125-mL, round-bottomed flask equipped with a magnetic stir bar was added acetate buffer (26 mL, 1 M aqueous solution, pH 5) under argon. Chlorodimethyl(3-methylbut-2-en-1-yl)silane (650 mg, 4.0 mmol) in diethyl ether (11 mL) was added via syringe and stirred. After 15 min the mixture was extracted with diethyl ether (3 x 100 mL) and combined organic extracts washed with $NaHCO_3$ (100 mL), water (100 mL), and Brine (100 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to a volume of 5 mL. The crude solution was purified immediately by column chromatography (pentane/diethyl ether (9:1), SiO_2, 20 mm x 100 mm) to remove silane impurities. The pure material was transferred as a solution in hexane (5 mL) to a single-necked round-bottomed flask. The solution was then added dropwise over 5 minutes to a Schlenk flask containing a slurry of KH (192 mg, 4.8 mmol, 1.2 equiv) in hexane (5 mL). Upon complete addition the reaction was allowed to stir for 30 minutes before filtering through a fritted glass funnel (medium porosity). The filtrate was concentrated *in vacuo* to afford 525 mg (72 %) white solid.

Data for **22**:

^{1}H NMR: (500 MHz, d_6-benzene)

5.48 (m, 1 H, HC(2)), 1.80 (s, 3 H, HC(4)), 1.70 (s, 3 H, HC(5)), 1.49 (d, J = 8.0, 2 H, HC(1)), 0.09 (s, 6 H, HC(1')).

General Procedure VII: Cross-coupling of Aryl bromides with potassium dimethyl(3-methylbut-2-en-1-yl)silanolate

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), and (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (15.2 mg, 0.03 mmol, 0.2 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of potassium dimethyl(3-methylbut-2-en-1-yl)silanolate (54.7 mg, 0.3 mmol, 2.0 equiv), aryl bromide (0.15 mmol) in toluene (0.3 mL) prepared in a glove box in a Schlenk flask was sealed and placed on a manifold where the headspace was evacuated and refilled with argon. The solution was then added to the reaction flask by canula. The resulting mixture was heated to 70 ºC in an oil bath and reaction progress monitored by GC. An aliquot of the reaction mixture was filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 2.

Table 7, Entry 1

Following General Procedure VII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (15.2 mg, 0.03 mmol, 0.2 equiv), potassium dimethyl(3-methylbut-2-en-1-yl)silanolate (54.7 mg, 0.3 mmol, 2.0 equiv), and 1-bromonaphthalene (31.1 mg, 0.15 mmol) in toluene (0.3 mL) was stirred at 70 ºC for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **15** γ-t_R= 7.96 min, α-t_R=8.74 min (10 % yield including both isomers, 1.6:1 α:γ ratio)

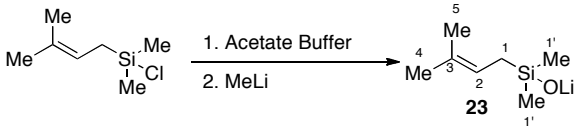
Table 7, Entry 2

Following General Procedure VII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (15.2 mg, 0.03 mmol, 0.2 equiv), potassium dimethyl(3-methylbut-2-en-1-yl)silanolate (54.7 mg, 0.3 mmol, 2.0 equiv), and 4-bromobenzophenone (39.2 mg, 0.15 mmol) in toluene (0.3 mL) was stirred at 70 ºC for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **16** γ-t_R= 11.50 min, α-t_R=12.09 min (20 yield including both isomers, 1:6 α:γ ratio)

Table 7, Entry 3

Following General Procedure VII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (15.2 mg, 0.03 mmol, 0.2 equiv), potassium dimethyl(3-methylbut-2-en-1-yl)silanolate (54.7 mg, 0.3 mmol, 2.0 equiv), and 4-bromobenzotrifluoride (33.7 mg, 0.15 mmol) in toluene (0.3 mL) was stirred at 70 ºC for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **18** γ-t_R= 3.31 min, α-t_R=4.11 min (25 % yield including both isomers, 2.2:1 α:γ ratio)

Preparation of Lithium Dimethyl(3-methylbut-2-en-1-yl)silanolate (23)



To a one-necked, 125-mL, round-bottomed flask equipped with a magnetic stir bar was added acetate buffer (26 mL, 1 M aqueous solution, pH 5) under argon. Chlorodimethyl(3-methylbut-2-en-1-yl)silane (650 mg, 4.0 mmol) in diethyl ether (11

mL) was added via syringe and stirred. After 15 min the mixture was extracted with diethyl ether (3 x 100 mL) and combined organic extracts washed with $NaHCO_3$ (100 mL), water (100 mL), and Brine (100 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to a volume of 5 mL. The crude solution was purified immediately by column chromatography (pentane/diethyl ether (9:1), SiO_2, 20 mm x 100 mm) to remove silane impurities. The pure material was transferred as a solution in hexane (5 mL) to a single-necked round-bottomed flask. The solution was then added dropwise over 5 minutes to a Schlenk flask containing methyl lithium (1.1 mL, 1.44 M in diethyl ether, 1.0 equiv) in ethyl ether (2.5 mL). Upon complete addition the reaction was allowed to stir for 30 minutes before filtering through a fritted glass funnel (medium porosity). The filtrate was concentrated *in vacuo* to afford 179 mg (75 %) white solid.

Data for **23**:

^{1}H NMR: (500 MHz, d_6-benzene)

5.21 (m, 1 H, HC(2)), 1.64 (s, 3 H, HC(4)), 1.54 (s, 3 H, HC(5)), 1.36 (d, J = 8.0, 2 H, HC(1)), -0.09 (s, 6 H, HC(1')).

General Procedure VIII: Cross-coupling of lithium dimethyl(3-methylbut-2-en-1-yl)silanolate with 4-bromobenzophenone

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), and (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.3 mg, 0.04 mmol, 0.2 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process

was repeated two additional times. A solution of lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromobenzophenone (52.2 mg, 0.2 mmol) in solvent (0.4 mL) prepared in a glove box in a Schlenk flask was sealed and placed on a manifold where the headspace was evacuated and refilled with argon. The solution was then added to the reaction flask by canula. The resulting mixture was heated in an oil bath and reaction progress monitored by GC. An aliquot of the reaction mixture was filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 2.

Table 8 Entry 1

Following General Procedure VIII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.3 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), and 4-bromobenzophenone (52.2 mg, 0.2 mmol) in toluene (0.4 mL) was stirred at 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **16** γ-t_R= 11.50 min, α-t_R=12.09 min (10 % yield including both isomers, 1:20 α:γ ratio)

Table 8 Entry 2

Following General Procedure VIII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.3 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), and 4-bromobenzophenone (52.2 mg, 0.2 mmol) in THF (0.4 mL) was stirred at refluxing temperatures in an oil bath for 24 h.

An aliquot of the reaction mixture was analyzed by GC method 2. **16** γ-t_R= 11.50 min, α-t_R=12.09 min (25 % yield including both isomers, 1:9 α:γ ratio)

Table 8 Entry 3

Following General Procedure VIII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.3 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), and 4-bromobenzophenone (52.2 mg, 0.2 mmol) in DME (0.4 mL) was stirred at 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **16** γ-t_R= 11.50 min, α-t_R=12.09 min (12 % yield including both isomers, 1:3.6 α:γ ratio)

Table 8 Entry 4

Following General Procedure VIII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.3 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), and 4-bromobenzophenone (52.2 mg, 0.2 mmol) in 1,4-dioxane (0.4 mL) was stirred at 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **16** γ-t_R= 11.50 min, α-t_R=12.09 min (45 % yield including both isomers, 1:26 α:γ ratio)

Table 8 Entry 5

Following General Procedure VIII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.3 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), and 4-bromobenzophenone (52.2 mg,

0.2 mmol) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **16** γ-t_R= 11.50 min, α-t_R=12.09 min (100 % yield including both isomers, 1:33 α:γ ratio)

Table 8 Entry 6

Following General Procedure VIII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(3,5-bis(trifluoromethyl)phenyl)penta-1,4-dien-3-one (20.3 mg, 0.04 mmol, 0.2 equiv), sodium dimethyl(3-methylbut-2-en-1-yl)silanolate (66.5 mg, 0.4 mmol, 2.0 equiv), and 4-bromobenzophenone (52.2 mg, 0.2 mmol) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **16** γ-t_R= 11.50 min, α-t_R=12.09 min (97 % yield including both isomers, 62:1 α:γ ratio)

General Procedure IX: Cross-Coupling of Lithium Dimethyl(3-methylbut-2-en-1-yl)silanolate with 4-Bromotoluene and Additives

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), and (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and additive in 1,4-dioxane (0.4 mL) prepared in a glove box in a Schlenk flask was sealed and placed on a manifold where the headspace was evacuated and refilled with argon.

The solution was then added to the reaction flask by canula. The resulting mixture was heated in an oil bath and reaction progress monitored by GC. An aliquot of the reaction mixture was filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 2.

Table 9 Entry 1

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and benzophenone (36.4 mg, 0.2 mmol, 1.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (25 % yield including both isomers, 1:12 α:γ ratio)

Table 9 Entry 2

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and THF (32 μL, 0.4 mmol, 2.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (30 % yield including both isomers, 1:35 α:γ ratio)

Table 9 Entry 3

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one

(14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and MeCN (21 μL, 0.4 mmol, 2.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (26 % yield including both isomers, 1:44 α:γ ratio)

Table 9 Entry 4

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and DME (42 μL, 0.4 mmol, 2.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (32 % yield including both isomers, 1:39 α:γ ratio)

Table 9 Entry 5

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and THF (65 μL, 0.8 mmol, 4.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (32 % yield including both isomers, 1:57 α:γ ratio)

Table 9 Entry 6

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and MeCN (42 μL, 0.8 mmol, 4.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (26 % yield including both isomers, 1:22 α:γ ratio)

Table 9 Entry 7

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and DME (83 μL, 0.8 mmol, 4.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (30 % yield including both isomers, 1:28 α:γ ratio)

Table 9 Entry 8

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and THF (162 μL, 2.0 mmol, 10.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath for 24

h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (31 % yield including both isomers, 1:11 α:γ ratio)

Table 9 Entry 9

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and THF (65 μL, 0.80 mmol, 4.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath in a sealed tube for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (36 % yield including both isomers, 1:47 α:γ ratio)

Table 9 Entry 10

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and THF (162 μL, 2.0 mmol, 10.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath in a sealed tube for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (37 % yield including both isomers, 1:33 α:γ ratio)

Table 9 Entry 11

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), and 4-bromotoluene (34.2 mg, 0.2 mmol) in 1,4-dioxane

(0.4 mL) was stirred at 120 ºC in an oil bath in a sealed tube for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (54 % yield including both isomers, 1:27 α:γ ratio)

Table 9 Entry 12

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and THF (65 μL, 0.80 mmol, 4.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 120 ºC in an oil bath in a sealed tube for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (30 % yield including both isomers, 1:17 α:γ ratio)

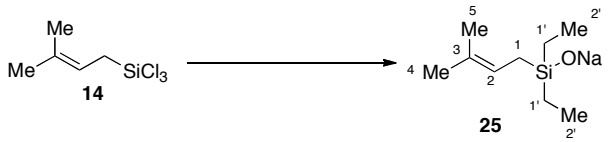
Table 9 Entry 13

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and THF (162 μL, 2.0 mmol, 10.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 120 ºC in an oil bath in a sealed tube for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (28 % yield including both isomers, 1:22 α:γ ratio)

Table 9 Entry 14

Following General Procedure IX, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv), lithium dimethyl(3-methylbut-2-en-1-yl)silanolate (60.1 mg, 0.4 mmol, 2.0 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and MeCN (42 μL, 0.80 mmol, 4.0 equiv) in 1,4-dioxane (0.4 mL) was stirred at 100 ºC in an oil bath in a sealed tube for 24 h. An aliquot of the reaction mixture was analyzed by GC method 2. **24** γ-t_R= 4.05 min, α-t_R=4.49 min (37 % yield including both isomers, 1:33 α:γ ratio)

Preparation of Sodium Diethyl(3-methylbut-2-en-1-yl)silanolate (25)



To a single-necked, 150-mL round-bottomed flask equipped with magnetic stir bar and addition funnel was charged **14** (3.445 g, 16.9 mmol) in THF (33 mL). The solution was stirred while ethyl magnesium bromide (14 mL, 33.8 mmol, 2 equiv. 2.42 M solution in diethyl ether) was added *via* the addition funnel over 20 minutes (internal temperature increased 15 ºC over course of addition). Upon complete addition of Grignard reagent the reaction was stirred under argon and heated to 65 ºC in an oil bath. After 4 h the reaction was cooled to room temperature and transferred (canula) to a single-necked 500-mL round-bottomed flask containing pH 5 acetate buffer (170 mL, 1 M solution) and stirred for 15 minutes. The mixture was extracted with diethyl ether (3 x 100 mL) and combined organic extracts washed with $NaHCO_3$ (100 mL), water (100 mL), and Brine (100 mL). The organic extract was dried over $MgSO_4$, filtered, and

concentrated *in vacuo* to a volume of 5 mL. The crude solution was purified immediately by column chromatography (pentane/diethyl ether (9:1), SiO_2, 20 mm x 20 cm) to remove silane impurities. The pure material was transferred as a solution in hexane (5 mL) to a single-necked round-bottomed flask. The solution was then added dropwise over 5 minutes to a Schlenk flask containing a slurry of NaH (487 mg, 20.3 mmol, 1.2 equiv) in hexane (20 mL). Upon complete addition the reaction was allowed to stir for 30 minutes before filtering through a fritted glass funnel (medium porosity). The filtrate was concentrated *in vacuo* to afford 2.3 g (70 %) white solid.

Data for **25**:

^{1}H NMR: (500 MHz, d_6-benzene)

5.50(m, 1 H, HC(2)), 1.80 (s, 3 H, HC(1)), 1.70 (s, 3 H, HC(4)), 1.52 (d, J = 8.5, HC(5)), 1.09 (t, J = 1.6, 6 H, HC(1')), 0.55 (m, 4 H, HC(2')).

^{13}C NMR: (126 MHz, C_6D_6)

128.3 (C(3)), 124.1 (C(2)), 25.9 (C(4)), 19.8 (C(5)), 17.8 (C(1)), 10.1 (C(1')), 8.4 (C(2')).

Scheme 20 Eq 1

Following general procedure XI, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv.), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv) a solution of sodium diethyl(3-methylbut-2-en-1-yl)silanolate (48.6 mg, 0.25 mmol, 1.25 equiv) and 4-bromobeznophenone (52.2 mg, 0.2 mmol) in 4 mL of toluene was stirred under argon at 70 ºC in an oil bath. . An aliquot of the reaction mixture was analyzed by GC method 3. **16** γ-t_R= 11.2 min, α-t_R=11.5 min (83 % yield including both isomers, 1:19 α:γ ratio)

Scheme 20 Eq 2

Following general procedure XI, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv.), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.04 mmol, 0.2 equiv) a solution of sodium diethyl(3-methylbut-2-en-1-yl)silanolate (48.6 mg, 0.25 mmol, 1.25 equiv) and 4-bromotoluene (34.2 mg, 0.2 mmol) in 4 mL of toluene was stirred under argon at 70 ºC in an oil bath. . An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.40 min, α-t_R=5.27 min (95 % yield including both isomers, 1:99 α:γ ratio)

General Procedure X: Cross-coupling of Sodium Diethyl(3-methylbut-2-en-1-yl)silanolate with 1-Bromonaphthalene

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added ligand and palladium precursor. The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of sodium diethyl(3-methylbut-2-en-1-yl)silanolate (78 mg, 0.4 mmol, 2 equiv), 1-bromonaphthalene (41.4 mg, 0.2 mmol) in toluene (0.4 mL) prepared in a glove box in a Schlenk flask was sealed and placed on a manifold where the headspace was evacuated and refilled with argon. The solution was then added to the reaction flask by canula. The resulting mixture was heated to 70 ºC in an oil bath and reaction progress monitored by GC. An aliquot of the reaction mixture was filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 3.

Table 10 Entry 1

Following General Procedure X, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), triphenylphosphine (5.2 mg, 0.02 mmol, 0.10 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (77.7 mg, 0.4 mmol, 2 equiv), and 1-bromonaphthalene (41.4 mg, 0.2 mmol) in toluene (0.4 mL) was heated to 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **15** γ-t_R= 8.14 min, α-t_R=8.80 min (60 % yield including both isomers, 1:3.3 α:γ ratio)

Table 10 Entry 2

Following General Procedure X, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), tri(2-furyl)phosphine (4.6 mg, 0.02 mmol, 0.10 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (77.7 mg, 0.4 mmol, 2 equiv), and 1-bromonaphthalene (41.4 mg, 0.2 mmol) in toluene (0.4 mL) was heated to 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **15** γ-t_R= 8.14 min, α-t_R=8.80 min (100 % yield including both isomers, 1:2.3 α:γ ratio)

Table 10 Entry 3

Following General Procedure X, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), triphenylarsine (6.1 mg, 0.02 mmol, 0.10 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (77.7 mg, 0.4 mmol, 2 equiv), and 1-bromonaphthalene (41.4 mg, 0.2 mmol) in toluene (0.4 mL) was heated to 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **15** γ-t_R= 8.14 min, α-t_R=8.80 min (21 % yield including both isomers, 1:10 α:γ ratio)

Table 10 Entry 4

Following General Procedure X, bis(dibenzylideneacetone)palladium (4.8 mg, 0.008 mmol, 0.05 equiv), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (12.3 mg, 0.033 mmol, 0.20 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (64.1 mg, 0.33 mmol, 2 equiv), and 1-bromonaphthalene (34.3 mg, 0.166 mmol) in toluene (0.33 mL) was heated to 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **15** γ-t_R= 8.14 min, α-t_R=8.80 min (100 % yield including both isomers, 1:20 α:γ ratio)

Table 10 Entry 5

Following General Procedure X, bis(dibenzylideneacetone)palladium (4.8 mg, 0.008 mmol, 0.05 equiv), tris(pentafluorophenyl)phosphine (8.8 mg, 0.016 mmol, 0.10 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (64.1 mg, 0.33 mmol, 2 equiv), and 1-bromonaphthalene (34.3 mg, 0.166 mmol) in toluene (0.33 mL) was heated to 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **15** γ-t_R= 8.14 min, α-t_R=8.80 min (< 5 % yield including both isomers, 1:22 α:γ ratio)

Table 10 Entry 6

Following General Procedure X, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), norbornadiene (0.92 mg, 1 μL, 0.01 mmol, 0.05 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (77.7 mg, 0.4 mmol, 2 equiv), and 1-bromonaphthalene (41.4 mg, 0.2 mmol) in toluene (0.4 mL) was heated to 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **15** γ-t_R= 8.14 min, α-t_R=8.80 min (100 % yield including both isomers, 1:4 α:γ ratio)

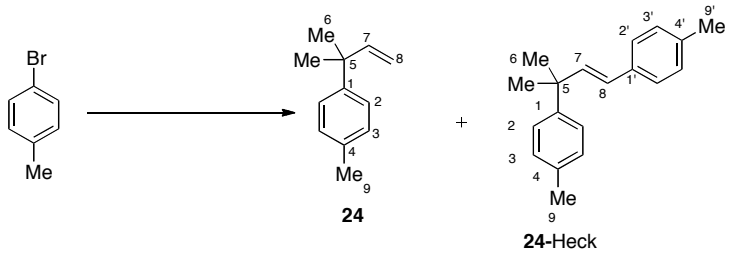
Table 10 Entry 7

Following General Procedure X, palladium(II) acetate (2.3 mg, 0.01 mmol, 0.05 equiv), tricyclohexylphosphine (11.2 mg, 0.04 mmol, 0.20 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (77.7 mg, 0.4 mmol, 2 equiv), and 1-bromonaphthalene (41.4 mg, 0.2 mmol) in toluene (0.4 mL) was heated to 70 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **15** γ-t_R= 8.14 min, α-t_R=8.80 min (0 % yield including both isomers)

General Procedure XI: Preparative Cross-coupling of Sodium Diethyl(3-methylbut-2-en-1-yl)silanolate and Aryl Bromides

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added bis(dibenzylideneacetone)palladium (28.8 mg, 0.05 mmol, 0.05 equiv) and (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (74 mg, 0.2 mmol, 0.2 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of sodium sodium diethyl(3-methylbut-2-en-1-yl)silanolate (242.9 mg, 1.25 mmol, 1.25 equiv), and aryl bromide, in toluene (4 mL) was added to the flask. The resulting mixture was heated to 70 ºC in an oil bath. After complete consumption of the bromide the reaction was then allowed to cool to room temperature. Diethyl ether (20 mL) was added and the mixture was filtered through a short pad of silica gel (5 g). The silica pad was washed with diethyl ether (100 mL) and the filtrates were concentrated *in vacuo* to afford the crude material. Purification by column chromatography followed by Kugelrohr distillation to afford the desired product.

Table 11 Entry 1: Preparation of 1-methyl-4-(2-methylbut-3-en-2-yl)benzene, (24)



Following General Procedure XI, bis(dibenzylideneacetone)palladium (28.8 mg, 0.05 mmol, 0.05 equiv.), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (74 mg, 0.2 mmol) a solution of sodium diethyl(3-methylbut-2-en-1-yl)silanolate (242.9 mg, 1.25 mmol, 1.25 equiv) and 4-bromotoluene (171 mg, 1 mmol) in 4 mL of toluene was stirred under argon at 110 ºC in an oil bath. After 22 h GC analysis indicated that no bromide remained and the reaction was allowed to cool to room temperature. Diethyl ether (15 mL) was added and the mixture was filtered through a pad of silica gel (5 g). The pad was rinsed with diethyl ether (100 mL) and the combined filtrates were concentrated *in vacuo* to afford 396 mg of crude material. Purified by column chromatography (hexane, SiO_2, 20 mm x 28 cm) and bulb-to-bulb distillation to afford 112 mg (70 %) colorless oil

Data for **24**:

bp: 110 ºC (17 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

7.28 (d, J = 8.0, 2 H, HC(3)), 7.15 (d, J = 8, 2 H, HC(2)), 6.05 (dd, J = 17.5 and 11, 1 H, HC(7)), 5.06 (m, 2 H, HC(8)), 2.35 (s, 3 H, HC(9)), 1.41 (s, 3 H, HC(6)).

^{13}C NMR: (126 MHz, $CDCl_3$)

148.2 (C(7)), 145.5 (C(1)), 135.1 (C(4)), 128.7 (C(3)), 125.9 (C(2)), 110.4 (C(8)), 40.7 (C(5)), 28.2 (C(6)), 20.8 (C(9)).

IR: (film)

3084 (m), 3023 (m), 2924 (s), 2967 (s), 2872 (m), 1901 (w), 1639 (w), 1513 (s), 1462 (m), 1412 (m), 1377 (m), 1360 (m), 1260 (w), 1190 (w), 1096 (s), 1005 (m), 911 (s), 815 (s)

GC: γ-t_R: 4.40 min (GC Method 3)

HRMS: (EI+, 70eV)

Calcd. for $C_{12}H_{16}(M^+)$: 160.12520; found: 160.12604

TLC: R_f= 0.39 (hexane) [silica gel, I_2]

Data for **24-Heck**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.26 (m, 4 H, HC(3'), HC(3), 7.12 (m, 4 H, HC(2), HC(2')), 6.36 (s, 2 H, HC(8), HC(7)), 3.33 (s, 6 H, HC(9), HC(9')), 1.48 (s, 6 H, HC(6)).

^{13}C NMR: (126 MHz, $CDCl_3$)

146.2 (C(1)), 139.6 (C(7)), 136.9 (C(1')), 135.6 (C(4)), 135.3 (C(4')), 129.4 (C(3)), 129.1 (C(3')), 126.4 (C(2)), 126.3 (C(2')), 126.0 (C(8)), 40.6 (C(5)), 29.1 (C(6)), 21.4 (C(9)), 21.1 (C(9')).

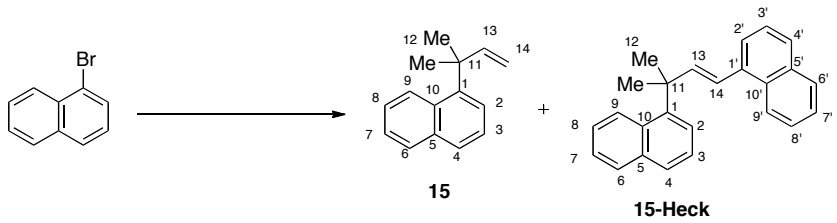
GC: γ-t_R: 10.98 min (GC Method 3)

MS: (EI+, 70eV)

250.2 (M^+, 72), 235.2 (100), 205.2 (21), 143.1 (70), 133.1 (86), 105.1 (34).

TLC: R_f= 0.22 (hexane) [silica gel, I_2]

Table 11 **Entry 2: Preparation of 1-(2-methylbut-3-en-2-yl)naphthalene, (15) and (15-Heck)**



Following General Procedure XI, bis(dibenzylideneacetone)palladium (28.8 mg, 0.05 mmol, 0.05 equiv.), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (74 mg, 0.2 mmol) a solution of sodium diethyl(3-methylbut-2-en-1-yl)silanolate (242.9 mg, 1.25 mmol, 1.25 equiv) and 1-bromonaphthalene (, 1 mmol) in 4 mL of toluene was stirred under argon at 110 ºC in an oil bath. After 22 h GC analysis indicated that no bromide remained and the reaction was allowed to cool to room temperature. Diethyl ether (15 mL) was added and the mixture was filtered through a pad of silica gel (5 g). The pad was rinsed with diethyl ether (100 mL) and the combined filtrates were concentrated *in vacuo* to afford 396 mg of crude material. Purified by column chromatography (hexane, SiO_2, 20 mm x 28 cm) and bulb-to-bulb distillation to afford 147 mg (70 %) colorless oil.

Data for **15**:

bp: 120 ºC (0.2 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

8.37 (d, *J* = 9.4, 1 H, HC(9)), 7.84 (m, 1 H, HC(2)), 7.78 (d, *J* = 8.2, 1 H, HC(4)), 7.55 (d, *J* = 7.1, 1 H, HC(6)), 7.42 (m, 3 H, HC(3), HC(7),

HC(8)), 6.30 (dd, J = 17.6 and 10.5, 1 H, HC(13)), 5.11 (m, 2 H, HC(14)), 1.64 (s, 6 H, HC(12)).

^{13}C NMR: (126 MHz, $CDCl_3$)

149.3 (C(13)), 143.9 (C(1)), 134.9 (C(5)), 131.5 (C(10)), 129.1 (C(6)), 127.7 (C(4)), 125.2 (C(3)), 124.8 (C(9)), 124.4 (C(7)), 123.5 (C(8), 111.5 (C(14)), 42.1 (C(11)), 30.0 (C(12)).

IR: (film)

3079 (m), 3048 (m), 2967 (s), 2874 (m), 1807 (w), 1631 (w), 1599 (m), 1508 (m), 1468 (m), 1396 (m), 1360 (m), 1240 (w), 1136 (m), 1009 (s), 910 (m), 801 (s), 777 (s)

GC: γ-t_R: 8.01 min (GC Method 3)

HRMS: (EI+, 70eV)

Calcd. for $C_{15}H_{16}(M^+)$: 196.12520; found: 196.12582

TLC: R_f= 0.31 (hexane) [silica gel, I_2]

Data for **15-Heck**:

^{1}H NMR: (500 MHz, $CDCl_3$)

8.52 (d, 1 H, J = 8.5 HC(9)), 7.88 (m, 2 H, HC(2), HC(9')), 7.83 (m, 2 H, HC(4), HC(2')), 7.74 (d, J = 8, 1 H, HC(4')), 7.66 (d, J = 7, 1 H, HC(6)), 7.45 (m, 7 H, HC(3'), HC(6'), HC(7'), HC(8'), HC(3), HC(7) HC(8)) 7.09 (d, J = 16, 1 H HC(14)), 6.70 (d, J = 16, 1 H, HC(13)), 1.84 (s, 3 H, HC(12)).

^{13}C NMR: (126 MHz, $CDCl_3$)

149.8 (C(aryl), 144.08 (C(aryl)), 135.9 (C(aryl)), 134.9 (C(aryl)), 133.5 (C(aryl)), 131.4 (C(aryl)), 131.2 (C(aryl)), 129.1 (C(aryl)), 128.3 (C(aryl)), 127.9 (C(aryl)), 127.7 (C(aryl)), 127.3 (C(aryl)), 125.7 (C(aryl)), 125.6 (C(aryl)), 125.6 (C(aryl)), 125.2 (C(aryl)), 124.9 (C(aryl)), 124.7 (C(aryl)), 124.5 (C(aryl/alkenyl)), 123.9 (C(aryl/alkenyl)), 123.6 (C(aryl/alkenyl)), 123.5 (C(aryl/alkenyl)), 42.1 (C(11)), 30.6 (C(12)).

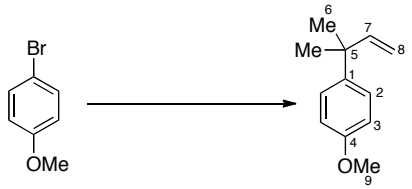
GC: γ-t_R: 10.98 min (GC Method 3)

MS: (EI+, 70eV)

322.2 (M^+, 2.1), 250.2 (6.7), 193.1 (14.5), 84.0 (100), 71.1 (35.2), 57.1 (83.8).

TLC: R_f= 0.22 (hexane) [silica gel, I_2]

Table 11 **Entry 3: Preparation of 1-methoxy-4-(2-methylbut-3-en-2-yl)benzene (19)**



19

Following General Procedure XI, bis(dibenzylideneacetone)palladium (28.8 mg, 0.05 mmol, 0.05 equiv.), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (74 mg, 0.2 mmol) a solution of sodium diethyl(3-methylbut-2-en-1-yl)silanolate (242.9 mg, 1.25 mmol, 1.25 equiv) and 4-bromoanisole (187 mg, 1 mmol) in 4 mL of toluene was stirred under argon at 110 ºC in an oil bath. After 22 h GC analysis indicated that no

bromide remained and the reaction was allowed to cool to room temperature. Diethyl ether (15 mL) was added and the mixture was filtered through a pad of silica gel (5 g). The pad was rinsed with diethyl ether (100 mL) and the combined filtrates were concentrated *in vacuo* to afford 396 mg of crude material. Purified by column chromatography (hexane/ethyl acetate (50:1), SiO_2, 20 mm x 28 cm) and bulb-to-bulb distillation to afford 100 mg (57 %) colorless oil.

Data for **19**:

bp: 140 ºC (17 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

7.28 (d, *J* = 8.5, 2 H, HC(3)), 6.86 (d, *J* = 9.0, 2 H, HC(2)), 6.02 (dd, *J* = 17.5 and 10.5, 1 H, HC(7)), 5.02 (dd, *J* = 10.5 and 17.5, 2 H, HC(8)), 3.80 (s, 3 H, HC(9)), 1.39 (s, 3 H, HC(6)).

^{13}C NMR: (126 MHz, $CDCl_3$)

157.6 (C(4)), 148.3 (C(7)), 140.6 (C(1)), 127.3 (C(3)), 113.4 (C(2)), 110.4 (C(8)), 55.2 (C(9)), 40.5 (C(5)), 28.4 (C(6))

IR: (film)

3082 (m), 2999 (m), 2965 (s), 2834 (m), 2873(m), 2040 (w), 1882 (w), 1637 (m), 1610 (m), 1512 (s), 1464 (m), 1297 (m), 1251 (s), 1182 (s), 1113 (m), 1037 (s), 912 (m), 829 (s)

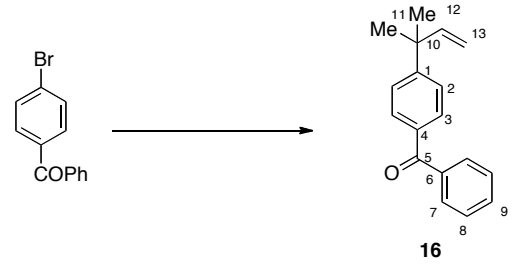
GC: γ-t_R: 5.78 min (GC Method 1)

HRMS: (EI+, 70eV)

Calcd. for $C_{12}H_{16}(M^+)$: 176.12012; found: 176.12089

TLC: R_f= 0.39 (hexane/EtOAc, 50:1) [silica gel, UV]

Table 11 Entry 4: Preparation of (4-(2-Methylbut-3-en-2-yl)phenyl)(phenyl)methanone (16)



16

Following General Procedure XI, bis(dibenzylideneacetone)palladium (28.8 mg, 0.05 mmol, 0.05 equiv.), (1*E*,4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (74 mg, 0.2 mmol) a solution of sodium diethyl(3-methylbut-2-en-1-yl)silanolate (242.9 mg, 1.25 mmol, 1.25 equiv) and 4-bromobeznophenone (261 mg, 1 mmol) in 4 mL of toluene was stirred under argon at 110 ºC in an oil bath. After 22 h GC analysis indicated that no bromide remained and the reaction was allowed to cool to room temperature. Diethyl ether (15 mL) was added and the mixture was filtered through a pad of silica gel (5 g). The pad was rinsed with diethyl ether (100 mL) and the combined filtrates were concentrated *in vacuo* to afford 396 mg of crude material. Purified by column chromatography (hexane/ethyl acetate (10:1), SiO_2, 20 mm x 28 cm) and bulb-to-bulb distillation to afford 162 mg (65 %) colorless oil.

Data for **16**:

bp: 210 ºC (17 mm Hg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

7.81 (m, 2 H, HC(7)), 7.75 (d, J = 8.5, 2 H, HC(3)), 7.59 (m, 1 H, HC(9)), 7.47 (m, 4 H, HC(8), HC(2)), 6.05 (dd, J = 10.5 and 18, 1 H, HC(12)), 5.11 (m, 2 H, HC(13))), 1.45 (s, 6 H, HC(11)).

^{13}C NMR: (126 MHz, $CDCl_3$)

196.4 (C(5)), 153.5 (C(6)), 147.1 (C(12)), 137.8 (C(4)), 135.1 (C(1)), 132.2 (C(7)), 130.1 (C(3)), 129.9 (C(2)), 128.3 (C(8)), 126.1 (C(9)), 111.5 (C(13)), 41. 5 (C(10)), 28.1 (C(11)).

IR: (film)

3083 (m), 2968 (s), 2872 (m), 1659 (s), 1603 (s), 1447 (m), 1405 (m), 1316 (s), 1278 (s), 1177 (m), 922 (s), 702 (s)

GC: γ-t_R: 11.2 min (GC Method 1)

HRMS: (EI+, 70eV)

Calcd. for $C_{18}H_{18}O(M^+)$: 250.13577; found: 250.13520

TLC: R_f= 0.39 (hexane/EtOAc, 10:1) [silica gel, UV]

General Procedure XII: Cross-coupling of Sodium Diethyl(3-methylbut-2-en-1-yl)silanolate with 4-Bromotoluene Using Different Solvents and Ligands

To an oven-dried, 5-mL, 1-piece round-bottomed flask/reflux condenser equipped with magnetic stir bar, septum and argon inlet was added ligand and bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv). The flask was then evacuated and refilled with argon, and this evacuation/refill process was repeated two additional times. A solution of sodium diethyl(3-methylbut-2-en-1-yl)silanolate (48.6 mg, 0.25 mmol, 1.25 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol), and biphenyl in solvent (2 mL) prepared in a glove box in a Schlenk flask was sealed and placed on a manifold where the headspace was evacuated and refilled with argon. The solution was then added to the reaction flask by canula. The resulting mixture was heated in an oil bath and reaction progress monitored by GC. An aliquot of the reaction mixture was

filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 3.

Table 12 Entry 1

Following General Procedure XII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*, 4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.4 mmol, 0.20 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (48.6 mg, 0.25 mmol, 1.25 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol) and biphenyl (11.0 mg, 0.0713 mmol) in 1,2-dimethoxy ethane (2 mL) was heated to 85 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (35 % yield including both isomers, 1:2 α:γ)

Table 12 Entry 2

Following General Procedure XII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*, 4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.4 mmol, 0.20 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (48.6 mg, 0.25 mmol, 1.25 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol) and biphenyl (11.0 mg, 0.0713 mmol) in THF (2 mL) was heated to 67 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (45 % yield including both isomers, 1:5 α:γ)

Table 12 Entry 3

Following General Procedure XII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*, 4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.4 mmol, 0.20 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate

(48.6 mg, 0.25 mmol, 1.25 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol) and biphenyl (11.1 mg, 0.0713 mmol) in 1,4-dioxane (2 mL) was heated to 100 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (65 % yield including both isomers, 1:30 α:γ)

Table 12 Entry 4

Following General Procedure XII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*, 4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.4 mmol, 0.20 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (48.6 mg, 0.25 mmol, 1.25 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol) and biphenyl (11.0 mg, 0.0713 mmol) in MeCN (2 mL) was heated to 81 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (9 % yield including both isomers, 99:1 α:γ)

Table 12 Entry 5

Following General Procedure XII, bis(dibenzylideneacetone)palladium (5.8 mg, 0.01 mmol, 0.05 equiv), (1*E*, 4*E*)-1,5-bis(4-(trifluoromethyl)phenyl)penta-1,4-dien-3-one (14.8 mg, 0.4 mmol, 0.20 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (48.6 mg, 0.25 mmol, 1.25 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol) and biphenyl (11.0 mg, 0.0713 mmol) in DMF (2 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (not detected)

Table 13 Entry 1

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), tricyclohexylphosphine (2.1 mg, 0.0075 mmol, 0.05

equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (8.9 mg, 0.0577 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (20 % yield of both isomers, only γ observed), **24**-Heck t_R=10.97 min (5 %)

Table 13 Entry 2

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), tri-*tert*-butylphosphine (1.5 mg, 0.0075 mmol, 0.05 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (14.5 mg, 0.0292 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (5 % yield of both isomers, only γ observed), **24-**Heck t_R=10.97 min (not observed)

Table 13 Entry 3

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (S-Phos) (3.1 mg, 0.0075 mmol, 0.05 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (11.7 mg, 0.0759 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (5% yield of both isomers, 3:1 α:γ), **24-**Heck t_R=10.97 min (not observed)

Table 13 Entry 4

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (X-Phos) (3.6 mg, 0.0075 mmol, 0.005 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (8.4 mg, 0.0545 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (50% yield of both isomers, 1:11 α:γ), **24-**Heck t_R=10.97 min (13 %)

Table 13 Entry 5

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), 2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl (RuPhos) (3.5 mg, 0.0075 mmol, 0.005 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (16.5 mg, 0.107 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (10% yield of both isomers, 1:1 α:γ), **24-**Heck t_R=10.97 min (5 %)

Table 13 Entry 6

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), tri(4-methoxyphenyl)phosphine (1.8 mg, 0.015 mmol, 0.1 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (7.7 mg, 0.0499 mmol) in

toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (65% yield of both isomers, 1:65 α:γ), **24-**Heck t_R=10.97 min (20 %)

Table 13 Entry 7

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), triphenylphosphine (3.9 mg, 0.015 mmol, 0.1 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (9.8 mg, 0.0635 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (25 % yield of both isomers, 1:31 α:γ), **24-**Heck t_R=10.97 min (7 %)

Table 13, Entry 8

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), tri(2-furyl)phosphine (3.5 mg, 0.015 mmol, 0.10 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (7.0 mg, 0.0454 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (15% yield of both isomers, 1:30 α:γ), **24-**Heck t_R=10.97 min (5 %)

Table 13, Entry 9

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), triethylphosphite (1.8 μL, 0.015 mmol, 0.1 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv),

4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (9.7 mg, 0.0629 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (50% yield of both isomers, 1:99 α:γ) **24-**Heck t_R=10.97 min (20 %)

Table 13, Entry 10

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), triethylphosphite (2.6 μL, 0.015 mmol, 0.1 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (9.7 mg, 0.0629 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **19** γ-t_R= 4.41 min, α-t_R=5.27 min (50% yield of both isomers, 1:99 α:γ), **19-**Heck t_R=10.97

Table 13, Entry 11

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), triphenylphosphite (3.9 μL, 0.015 mmol, 0.1 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (9.7 mg, 0.0629 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (30% yield of both isomers, 1:90 α:γ), **24-**Heck t_R=10.97 min (26 %)

Table 13, Entry 12

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), triphenylarsine (4.6 mg, 0.015 mmol, 0.10 equiv), sodium

diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (8.4 mg, 0.0545 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (60% yield of both isomers, 1:99 α:γ), **24-**Heck t_R=10.97 min (7 %)

min (18 %)

Table 13, Entry 13

Following General Procedure XII, allylpalladium chloride dimer (1.4 mg, 0.00375 mmol, 0.025 equiv), triphenylarsine (4.6 mg, 0.015 mmol, 0.1 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (9.7 mg, 0.0629 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (60 % yield of both isomers, 1:46 α:γ), **24-**Heck t_R=10.97 min (6 %)

Table 13, Entry 14

Following General Procedure XII, allylpalladium chloride dimer (1.8 mg, 0.005 mmol, 0.025 equiv), triphenyantimony (7.1 mg, 0.02 mmol, 0.10 equiv) sodium diethyl(3-methylbut-2-en-1-yl)silanolate (48.6 mg, 0.25 mmol, 1.25 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol) and biphenyl (6.8 mg, 0.0440 mmol) in toluene (0.8 mL) was heated to 110 ºC in an oil bath for 3 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (40 % yield of both isomers, 1:99 α:γ), **24-**Heck t_R=10.97 min (10 %)

Table 13, Entry 15

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), tri(pentafluorophenyl)phosphine (8.0 mg, 0.015 mmol, 0.1 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (9.8 mg, 0.0635 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (20 % yield of both isomers, only γ), **24-**Heck t_R=10.97 min (5 %)

Table 13, Entry 16

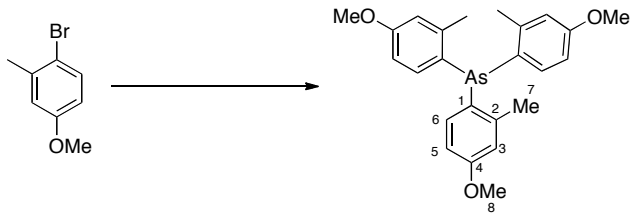
Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), 1,2-bis(diphenylphosphino)ethane monoxide (3.1 mg, 0.0075 mmol, 0.05 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (9.8 mg, 0.0635 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (40 % yield of both isomers, 1:99 α:γ), **24-**Heck t_R=10.97 min (12 %)

Table 13, Entry 17

Following General Procedure XII, bis(dibenzylideneacetone)palladium (4.3 mg, 0.0075 mmol, 0.05 equiv), 1,2-bis(diphenylphosphino)propane monoxide (3.2 mg, 0.0075 mmol, 0.05 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (34.2 mg, 0.176 mmol, 1.25 equiv), 4-bromotoluene (24.2 mg, 0.141 mmol) and biphenyl (9.8 mg, 0.0635 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An

aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (35 % yield of both isomers, 1:99 α:γ), **24-**Heck t_R=10.97 min (22 %).

Preparation of Tris(4-methoxy-2-methylphenyl)arsine (26)



26

To a single-necked, 50-mL, round-bottomed flask equipped with a magnetic stir bar and reflux condenser was added Mg turnings (401 mg, 16.5 mmol, 1.1 equiv.) and LiCl (635 mg, 15 mmol, 1.0 equiv.) and THF (2 mL) under argon. 4-Bromo-3-methyl-anisole (0.5 g, 2.5 mmol) added dropwise by pipette until reaction initiated. Remaining 4-bromo-3-methyl-anisole (2.516 g, 12.5 mmol, 3.03 equiv. in total) added as solution in THF (8 mL) at a rate to maintain refluxing conditions. Upon complete addition the reaction was stirred under argon at 67 ºC in an oil bath. After 4 h the reaction was allowed to cool to room temperature and canula filtered to a single-necked 50-mL round-bottomed flask containing a magnetic stir bar. The flask was cooled to 0 ºC in an ice bath while arsenic(III) chloride (0.416 mL, 4.94 mmol) was added dropwise with a syringe over 5 minutes. The reaction was allowed to slowly warm to room temperature over 12 h before water (16 mL) was added and stirred for 30 minutes. The mixture was extracted with diethyl ether (3 x 50 mL) and the combined organic extracts were washed with Brine (20 mL), combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield a beige solid. Purification by recrystallization in methanol to afford 1.2 g (57 %) white solid.

Data for **26**:

mp: 195 ºC

^{1}H NMR: (500 MHz, $CDCl_3$)

6.80 (d, *J* = 2.5, 3 H, HC(3)), 6.70 (d, *J* = 8.5, 3 H, HC(6)), 6.63 (dd, *J* = 3.0 and 8.5, 3 H, HC(5)), 3.79 (s, 9 H, HC(8)), 2.39 (s, 9 H, HC(7)).

^{13}C NMR: (126 MHz, $CDCl_3$)

159.9 (C(4)), 143.8 (C(2)), 134.4 (C(3)), 128.7 (C(1)), 115.7 (C(6)), 111.6 (C(5)), 55.0 (C(8)), 22.1 (C(7))

IR: (film)

3055 (w), 3007 (w), 2962 (w), 2841 (w), 1589 (m), 1480 (m), 1301 (m), 1235 (s), 1152 (m), 1048 (s), 813 (w)

MS: (EI+, 70eV)

438 (M^+, 100), 317 (31), 240 (32), 196 (39), 121 (20.3)

Scheme 23

Following General Procedure XII, allylpalladium chloride dimer (1.8 mg, 0.005 mmol, 0.025 equiv), # (8.8 mg, 0.02 mmol, 0.1 equiv), sodium diethyl(3-methylbut-2-en-1-yl)silanolate (48.2 mg, 0.25 mmol, 1.25 equiv), 4-bromotoluene (34.2 mg, 0.2 mmol) and biphenyl (15.3 mg, 0.0992 mmol) in toluene (0.6 mL) was heated to 110 ºC in an oil bath for 24 h. An aliquot of the reaction mixture was analyzed by GC method 3. **24** γ-t_R= 4.41 min, α-t_R=5.27 min (60 % yield of both isomers, 1:99 α:γ), **24-Heck** t_R=10.97 min (15 %)

5.4. Chapter 4 Procedures

GC Methods and Response Factors

GC Method 1: Injections were made onto a Hewlett-Packard HP1 30-m capillary column. The injector temperature was 250 ºC and detector temperature was 300 ºC with a H_2 carrier gas flow of 16 mL/min. The column over temperature was as follows 100 ºC for 1 min, 100 ºC to 250 ºC ramp at 20 ºC/min, 250 ºC for 3 min, total run time 13.5 min. Response factors (R_f) for quantitative GC analysis for GC Method 1 were obtained by the equation below:

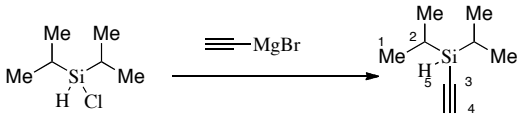
Eq1: Response factor for A = (area A * mmol naphthalene)/ (mmol A * area naphthalene)

mmol Naphthalene	Area Naphthalene	mmol 4-bromotoluene	Area 4-bromotoluene	Response Factor
0.0834	497349	0.0649	263713	0.68
0.0834	495883	0.0649	262967	0.68
0.0834	503955	0.0649	267110	0.68
0.226	831110	0.0585	140141	0.65
0.226	827041	0.0585	139504	0.65
0.226	824475	0.0585	139421	0.65
0.0913	229246	0.117	199614	0.67
0.0913	229197	0.117	199780	0.68
0.0913	220519	0.117	192327	0.68
			Avg.	0.67

GC/MS Method D: Injections were made onto a Hewlett-Packard HP1MS 30-m capillary column. The injector temperature was 250 ºC and detector temperature was 280 ºC with a H_2 carrier gas flow of 64 mL/min. The column over temperature was as follows 100 ºC for 3 min, 100 ºC to 300 ºC ramp at 40 ºC/min, 300 ºC for 2.5 min, total run time 10.5 min.

GC/MS Method E: Injections were made onto a Hewlett-Packard HP1MS 30-m capillary column. The injector temperature was 250 ºC and detector temperature was 300 ºC with a H_2 carrier gas flow of 37 mL/min. The column over temperature was as follows 100 ºC for 3 min, 100 ºC to 300 ºC ramp at 40 ºC/min, 300 ºC for 5.5 min, total run time 13.5 min.

Preparation of Ethynyldiisopropylsilane (36)



36

To a three-necked, 150-mL round-bottomed flask equipped with a magnetic stir bar was added diisopropylchlorosilane (5 g, 33.18 mmol) in THF (17 mL) under argon. The solution was then cooled to 0 ºC. To the solution was added ethynyl magnesium bromide (70 mL, 0.5 M in THF, 35 mmo, 1.05 equiv) dropwise over 30 minutes. The reaction was then allowed to warm to room temperature and stirred. After 2 h the reaction was quenched with 100 mL hexane and the resulting mixture was filtered through Celite (15 g). The filtrate was concentrated at 1 atm and the crude distilled to afford 3.49 g (75 %) colorless oil.

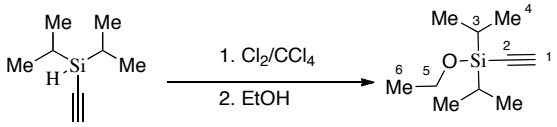
Data for **36**:

bp: 110 º C (760 mm Hg)

^{1}H NMR: (500 MHz, $CDCl_3$)

3.70 (s, 1 H, HSi(5)), 2.40 (s, 1 H, HC(4)), 1.04 (m, 14 H, HC(1), HC(2))

Preparation of Ethoxy(ethynyl)diisopropylsilane (37)



37

To a three-necked, 100 mL, round-bottomed flask equipped with a magnetic stir bar was added ethynyldiisopropylsilane (1.9 g, 13.5 mmol) in CH_2Cl_2 (13.5 mL) under argon. The solution was then cooled to 0 ºC. To the solution was added Cl_2 (14.4 mL, 1.13 M in CCl_4, 16.25 mmol, 1.2 equiv) dropwise. The reaction was then allowed to warm to room temperature and stirred. After 30 minutes triethylamine (4.7 mL, 33.75 mmol, 2.5 equiv) and ethanol (3.9 mL, 67.5 mmol, 5.0 equiv) was added and stirred. After 2 hours the reaction was quenched with 100 mL hexane and the resulting mixture was filtered through Celite (15 g). The filtrate was concentrated at 1 atm and the crude distilled to afford 2.24 g (90 %) colorless oil.

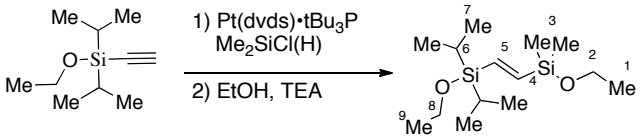
Data for **37**:

bp: 120 º C (100 mm Hg)

^{1}H NMR: (500 MHz, $CDCl_3$)

3.84 (q, J = 6.5, 2 H, HC(5)), 2.41 (s, 1H, HC(1)), 1.21 (t, J = 7, 3 H, HC(6)), 1.50 (m, 14 H HC(3), HC(4))

Preparation of (*E*)-4,4-Diisopropyl-7,7-dimethyl-3,8-dioxa-4,7-disiladec-5-ene (38)



38

To a one-necked, 250 mL, round-bottomed flask equipped with a magnetic stir bar was added dimethylchlorosilane (0.816 g, 8.62 mmol, 1.25 equiv) and platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane tri(*tert*-butyl)phosphine complex (71 μL, 0.12 M in xylenes, 8.61 μmol, 0.0015 equiv) in diethyl ether (15 mL) under argon. The solution was then heated to reflux. To the solution was added ethoxy(ethynyl)diisopropylsilane (1.06 g, 5.74 mmol) in diethyl ether (14 mL) dropwise over 5 minutes. After 2 hours the reaction was canula transferred to a one-necked, 250 mL, round-bottomed flask containing ethanol (1.7 mL, 28.7 mmol, 5 equiv), triethylamine (2.0 mL, 14.35 mmol, 2.5 equiv) in THF (12 mL) at 0 ºC. After transfer was complete the mixture was allowed to warm to room temperature. After 2 hours the reaction was quenched with 100 mL hexane and the resulting mixture was filtered through Celite (15 g). The filtrate was washed with water (3 x 50 mL) and the combined organic extracts were washed with Brine (50 mL), dried of $MgSO_4$ and concentrated *in vacuo* to afford a gold oil. Purification by fractional distillation to yield 1.26 g (76 %) colorless oil.

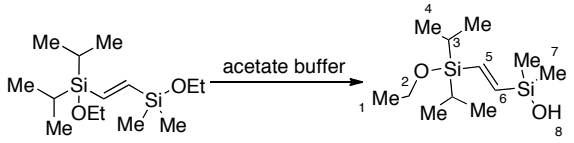
Data for **38**:

bp: 120 º C (0.2 mm Hg)

^{1}H NMR: (500 MHz, $CDCl_3$)

6.73 (d, J = 23, 1 H, HC(4)), 6.64 (d, J = 23, 1 H, HC(5)), 3.78 (q, J = 6.5, 2 H, HC(8)), 3.69 (q, J = 7.0, 2 H, HC(2)), 1.22 (m, 6 H, HC(1), HC(9)), 1.05 (m, 14 H, HC(6), HC(7)), 0.21 (s, 6 H, HC(3)).

Preparation of (*E*)-(2-(Ethoxydiisopropylsilyl)vinyl)dimethylsilanol (35)



35

To a one-necked, 100-mL, round-bottomed flask equipped with a magnetic stir bar was added acetate buffer (14.75 mL, 1 M aqueous solution, pH 5, 6.0 equiv) and under argon. To the solution was added (*E*)-4,4-diisopropyl-7,7-dimethyl-3,8-dioxa-4,7-disiladec-5-ene (711 mg, 2.46 mmol) in acetonitrile (14.75 mL) dropwise. After 5 hours the reaction was extracted with hexane (3 x 100 mL) and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 m), (Brine (50 mL), dried of $MgSO_4$ and concentrated *in vacuo* to afford a colorless oil. Purification by Kugelrohr distillation to afford a colorless oil.

Data for **35**:

bp: 100 º C (0.2 mm Hg)

^{1}H NMR: (500 MHz, $CDCl_3$)

6.75 (d, J = 23, 1 H, HC(6)), 6.63 (d, J = 23, 1 H, HC(5)), 3.76 (q, J = 6.5, 2 H, HC(2)), 3.69 (q, J = 7.0, 2 H, HC(2)), 1.21 (t, J = 7, 3 H, HC(1)), 1.03 (m, 14 H, HC(3), HC(4)), 0.23 (s, 6 H, HC(7)).

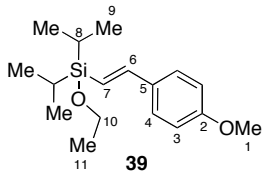
IR: (film)

3294 (br), 2944 (s), 3867(s), 1463 (m), 1389 (m), 1251 (s), 1172 (s), 1110 (s), 1017 (s) 881 (s) 751 (s), 660 (m)

General Procedure XIII: Cross-coupling of (*E*)-(2-(Ethoxydiisopropylsilyl)vinyl)dimethylsilanol with Aryl Halides

To a two-necked, 5-mL, Schlenk flask was added KH in THF under argon. To the slurry was added dropwise **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol in THF. After 30 minutes the mixture was filtered vis canula transferred to a one-necked, 5-mL, round-bottomed flask equipped with stirbar and reflux condenser containing palladium source, ligand, and aryl halide under an inert atmosphere and the reaction progress monitored by GC. An aliquot of the reaction mixture was quenched onto acetate buffer (1 mL, 1M, pH 5) and filtered through a small amount of silica gel eleuted with diethyl ether and analyzed by GC method 1.

Scheme 33 Preparation of (*E*)-ethoxydiisopropyl(4-methoxystyryl)silane (39)



39

Following General Procedure XIII, KH (7.6 mg, 0.19 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (50 mg, 0.19, 1.2 equiv), bis(dibenzylideneacetone)palladium (4.6 mg, 0.008 mmol, 0.05 equiv), TMSOK (10.3 mg, 0.08 mmol, 0.5 equiv) and 4-iodoanisole (38 mg, 0.16 mmol) in THF (0.2 mL) was stirred under argon. After 4 hours no iodide was remaining and the reaction was taken up in ethyl acetate (5 mL) and the organic layer was washed with water (25 mL), Brine (20

mL), dried of Na_2SO_4, filtered, and concentrated *in vacuo* to afford an organe solid. Purification by column chromatography (hexane/ethyl acetate (99/1), SiO_2, 20 mm x 100 mm) to yield 21 mg (45 %) colorless oil.

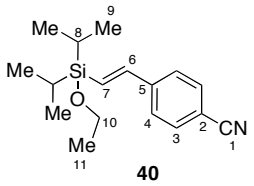
Data for **39**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.42 (d, J = 8.5, 2 H, HC(4)), 7.00 (d, J = 19.5, 1 H, HC(6)), 6.89 (d, J = 8.5, 2 H, HC(3)), 6.20 (d, J = 19.5, 1 H, HC(7)), 3.81 (m, 5 H, HC(1), HC(10)), 1.24 (t, J = 7.5, 3 H, HC(11)), 1.07 (m, 14 H, HC(8), HC(9)).

TLC: R_f= 0.35 (hexane/EtOAc, 19:1) [silica gel, UV]

Scheme 35 eq. 1 Preparation of (*E*)-4-(2-(Ethoxydiisopropylsilyl)vinyl)benzonitrile (40)



40

To a one-necked, 5-mL , round-bottomed flask equipped with magnetic stir bar was added bis(dibenzylideneacetone)palladium (2.5 mg, 0.0043 mmol, 0.05 equiv),), 4-iodobenzonitrile (23 mg, 0.1 mmol) and **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26 mg, 0.1 mmol, 1.0 equiv) under argon. A solution of TMSONa (22.4 mg, 0.2 mmol, 2.0 equiv) in THF (0.2 mL) was added and reaction stirred at room temperature under argon. After 4 h, ethyl acetate (5 mL) was added and mixture quenched onto acetate buffer (10 mL, 1 M aqueous, pH 5). The organic extracts were washed with brine (10 mL), dried with Na_2SO_4, filtered, and concentrated *in vacuo* to yield a dark oil. Product was observed by ^{1}H NMR.

Data for **40**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.64 (d, *J* = 8.5, 2 H, HC(3)), 7.54 (d, *J* = 8.5, 2 H, HC(4)), 7.06 (d, *J* = 19.5, 1 H, HC(6)), 6.53 (d, *J* = 19.5, 1 H, HC(7)), 3.80 (q, *J* = 6.5, 2 H, HC(10)), 1.25 (t, *J* = 6.5, 3 H, HC(11)), 1.06 (m, 14 H, HC(8), HC(9)).

GC/MS: (Method E)

t_R= 11.8 min/ 287 (M^+)

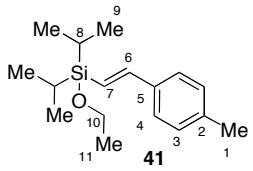
Scheme 35 eq. 2

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), and 4-iodobenzonitrile (23 mg, 0.1 mmol) in THF (0.2 mL) was stirred at room temperature for 8 h. An aliquot of the reaction mixture was analyzed by GC/MS method E: **41** t_R= 11.83 min, 287 (M^+). (70 %)

Scheme 25 eq 3.

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), and 4-iodotoluene (21.8 mg, 0.1 mmol) in THF (0.2 mL) was stirred at room temperature for 8 h. An aliquot of the reaction mixture was analyzed by GC/MS method E: **41** no product detected.

Scheme 36 eq 1: Preparation of (*E*)-Ethoxydiisopropyl(4-methylstyryl)silane (41)



41

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), 4-iodotoluene (21.8 mg, 0.1 mmol) and potassium hydroxide (1.4 mg, 0.025 mmol, 0.25 equiv) in THF (0.2 mL) was stirred at room temperature. After 8 h, ethyl acetate (5 mL) was added and mixture quenched onto acetate buffer (10 mL, 1 M aqueous, pH 5). The organic extracts were washed with Brine (10 mL), dried with Na_2SO_4, filtered, and concentrated *in vacuo* to yield a dark oil. Product was observed by ^{1}H NMR.

Data for **41**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.34 (d, J = 8.0, 2 H, HC(4)), 7.15 (d, J = 8.0, 2 H, HC(3)), 7.03 (d, J = 18.5, 1 H, HC(6)), 6.31 (d, J = 18.5, 1 H, HC(7)), 3.82 (q, J = 6.5, 2 H, HC(10)), 2.35 (s, 3 H, HC(1), 1.25 (t, J = 6.5, 3 H, HC(11)), 1.06 (m, 14 H, HC(8), HC(9)).

GC/MS: (Method E)

t_R= 7.99 min/ 276 (M^+)

GC: (Method 1)

t_R= 7.83 min

Scheme 36 eq 2

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), and 4-iodotoluene (21.8 mg, 0.1 mmol) in THF (0.2 mL) was stirred at reflux for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (70 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 1

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), triphenylphosphine (3 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 7 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (40 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 2

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), tri(4-methoxyphenyl)phosphine (3.5 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (5 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 3

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), tri(2-tolyl)phosphine (3.7 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (1 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 4

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), tricyclohexylphosphine (2.8 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected)

Table 14 Entry 5

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 2-(Di-*tert*-butylphosphino)biphenyl (1.5 mg, 0.005 mmol, 0.05 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction

mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected)

Table 14 Entry 6

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (2 mg, 0.005 mmol, 0.05 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (10 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 7

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), (2-methoxyphenyl)diphenylphosphine (3.5 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (40 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 8

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 2-(diphenylphosphino)phenol (3.5 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2

mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (15 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 9

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), tri(pentafluorophenyl)phosphine) (5.3 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (5 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 10

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,2-bis(diphenylphosphino)ethane (2 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (10 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 11

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,3-

bis(diphenylphosphino)propane (10 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (50 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 12

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,5-bis(diphenylphosphino)pentane (2.1 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (30 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 13

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,1'-bis(diphenylphosphino)ferrocene (2.8 mg, .005 mmol, 0.05 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (23 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 14

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv),

bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected)

Table 14 Entry 15

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), tricphenylphosphine (2.6 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (15 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 16

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), 1,3-bis(diphenylphosphino)propane (2.0 mg, 0.005 mmol, 0.05 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected)

Table 14 Entry 17

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv),

bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), (2-methoxyphenyl)diphenylphosphine (3.5 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected)

Table 14 Entry 18

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), (1*E*,4*E*)-1,5-bis(4-methoxyphenyl)penta-1,4-dien-3-one)palladium (4.2 mg, 0.005 mmol, 0.05 equiv), and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected)

Table 14 Entry 19

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), (1*E*,4*E*)-1,5-bis(4-methoxyphenyl)penta-1,4-dien-3-one)palladium (4.2 mg, 0.005 mmol, 0.05 equiv), triphenylphosphine (4.0 mg, 0.010 mmol, 0.1 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (10 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 14 Entry 20

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), (1*E*,4*E*)-

1,5-bis(4-methoxyphenyl)penta-1,4-dien-3-one)palladium (4.2 mg, 0.005 mmol, 0.05 equiv), 1,3-bis(diphenylphosphino)propane (2. mg, 0.005 mmol, 0.05 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (15 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 15 Entry 1

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), triphenylphosphine (3 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at reflux for 7 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (20 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 15 Entry 2

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,3-bis(diphenylphosphino)propane (2.0 mg, 0.005 mmol, 0.05 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at reflux for 7 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (18 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 15 Entry 3

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), (2-methoxyphenyl)diphenylphosphine (3.5 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at reflux for 7 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (11 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 15 Entry 4

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), triphenylphosphine (3 mg, .010 mmol, 0.10 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at reflux for 7 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (5 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 15 Entry 5

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv bis(dibenzylideneacetone)palladium (2.8 mg, 0.005 mmol, 0.05 equiv), 1,3-bis(diphenylphosphino)propane (2.0 mg, 0.005 mmol, 0.05 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at reflux for 8 h. An aliquot of the

reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (2 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 16 Entry 1

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,3-bis(diphenylphosphino)propane (2.0 mg, 0.005 mmol, 0.05 equiv), potassium hydroxide (1.3 mg, 0.02 mmol, 0.2 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at room temperature for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected).

Table 16 Entry 2

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), triphenylphosphine (3 mg, .010 mmol, 0.10 equiv) potassium hydroxide (1.3 mg, 0.02 mmol, 0.2 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at room temperature for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected).

Table 16 Entry 3

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 2-

dicyclohexylphosphino-2',6'-dimethoxybiphenyl (2 mg, 0.005 mmol, 0.05 equiv) potassium hydroxide (1.3 mg, 0.02 mmol, 0.2 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at room temperature for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected).

Table 16 Entry 4

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,3-bis(diphenylphosphino)propane (2.0 mg, 0.005 mmol, 0.05 equiv), potassium hydroxide (1.3 mg, 0.02 mmol, 0.2 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (98 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 16 Entry 5

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,3-bis(diphenylphosphino)propane (2.0 mg, 0.005 mmol, 0.05 equiv), potassium carbonate (2.8 mg, 0.02 mmol, 0.2 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (55 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 16 Entry 6

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (2 mg, 0.005 mmol, 0.05 equiv) potassium hydroxide (1.3 mg, 0.02 mmol, 0.2 equiv) and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 8 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (65 % yield) GC/MSt_R= 7.99 min, 276 (M^+)

Table 17 Entry 1

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,1-bis(diphenylphosphino)methane oxide (2.0 mg, 0.005 mmol, 0.05 equiv), and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (25 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 17 Entry 2

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,2-bis(diphenylphosphino)ethane monoxide (2.1 mg, 0.005 mmol, 0.05 equivand 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An

aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (61 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 17 Entry 3

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,3-bis(diphenylphosphino)propane monoxide (2.1 mg, 0.005 mmol, 0.05 equiv), and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (55 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 17 Entry 4

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,4-bis(diphenylphosphino)butane monoxide (2.2 mg, 0.005 mmol, 0.05 equiv), and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (85 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 17 Entry 5

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), triphenylphosphine oxide (1.4 mg, 0.005 mmol, 0.05 equiv), and 4-bromotoluene (17.2 mg, 0.1 mmol) in

THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (no product detected).

Table 17 Entry 6

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,1'-bis(diphenylphosphanyl) ferrocene monoxide (2.8 mg, 0.005 mmol, 0.05 equiv), and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (5 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 17 Entry 7

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl monoxide (3.2 mg, 0.005 mmol, 0.05 equiv), and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (5 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Table 17 Entry 8

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E***)**-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,2-

bis(diphenylphosphino)ethane oxide (2.2 mg, 0.005 mmol, 0.05 equiv), and 4-bromotoluene (17.2 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **41** GC: t_R= 7.83 min (50 % yield) GC/MSt_R= 7.99 min, 276 (M^+).

Scheme 37 eq. 1

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,4-bis(diphenylphosphino)butane monoxide (2.2 mg, 0.005 mmol, 0.05 equiv), and 4-bromobenzonitrile (19.9 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **40** GC: t_R= (no product detected).

Scheme 37 eq. 2

Following General Procedure XIII, KH (4.8 mg, 0.12 mmol, 1.2 equiv), **(***E*)-(2-(ethoxydiisopropylsilyl)vinyl)dimethylsilanol (26.1 mg, 0.1, 1.0 equiv), allylpalladium chloride dimer (0.91 mg, 0.0025 mmol, 0.025 equiv), 1,4-bis(diphenylphosphino)butane monoxide (2.2 mg, 0.005 mmol, 0.05 equiv), and 4-bromoacetophenone (19.9 mg, 0.1 mmol) in THF (0.2 mL) was stirred at 50 ºC for 18 h. An aliquot of the reaction mixture was analyzed by GC (method 1) and GC/MS method D: **42** GC: t_R= (no product detected).

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